

The Affordable Medicines Facility-malaria in Ghana: Factors Accounting for
Antimalarial Availability and Pricing Outcomes

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Dedication

This thesis is dedicated to my wife, Ama Amuasi.

Table of Contents

List of Tables	vi
List of Figures	vii
List of Appendices	viii
List of Definitions and Abbreviations	xi
Chapter 1: Specific Aims	1
Chapter 2: Statement of Purpose and Background	4
<i>Introduction</i>	<i>4</i>
<i>Antimalarial Policy</i>	<i>4</i>
<i>The Affordable Medicines Facility – malaria</i>	<i>6</i>
<i>Implementation of the AMFm</i>	<i>7</i>
<i>The AMFm Independent Evaluation and its limitations</i>	<i>8</i>
Purpose of the Dissertation	10
Theory and Conceptual Model	10
The data set	13
Importance of the dissertation to malaria research	16
Chapter 3: The AMFm in Ghana: Exploring Training and other Factors as Predictors of Stocking Practices	19
Introduction	19
Background	20
Methods	24
<i>Data source</i>	<i>24</i>
<i>Data management</i>	<i>25</i>
<i>Variables</i>	<i>26</i>
<i>Statistical Approach</i>	<i>26</i>
Results	27
<i>Outlet characteristics</i>	<i>27</i>
<i>Training and antimalarial stocking practices</i>	<i>29</i>
<i>Predicted probability of stocking QAACts after adjusting for other Covariates</i>	<i>30</i>

Discussion	32
Chapter 4: The AMFm in Ghana: Factors Associated with Private Retailer's	
Adherence to the Recommended Retail Price	48
Introduction.....	48
Background	50
Methods	53
<i>Data Source</i>	53
<i>Data Management</i>	54
<i>Variables</i>	55
<i>Statistical Approach</i>	56
Results	58
<i>Outlet Characteristics</i>	58
<i>Stocking and sales volume</i>	59
<i>Malaria prevalence and epidemiologic zones</i>	60
Discussion	61
Chapter 5: The Impact of Training on Knowledge of the Recommended Retail Price	
for AMFm Co-paid Antimalarials in Urban and Rural	
Outlets in Ghana	79
Introduction	79
Background	82
Methods	85
<i>Data Source</i>	85
<i>Data Management</i>	86
<i>Variables</i>	87
<i>Statistical Approach</i>	87
Results	88
<i>Private Sector Outlet Characteristics</i>	88
<i>Training, Urban/Rural Location and Knowledge</i>	89
<i>Malaria prevalence and epidemiologic zones</i>	90
Discussion	91

Chapter 6: Conclusions and Future Implications	102
<i>Predictors of Stocking QAACTs</i>	<i>104</i>
<i>Adherence to the Recommended Retail Price</i>	<i>105</i>
<i>Urban-rural Variations in the impact of training on knowledge</i>	<i>107</i>
Bibliography	109
Appendices	121

List of Tables

Table 1: Distribution of outlet and respondent characteristics in AMFm IE dataset	15
Table 2: Independent variables	42
Table 3: Unweighted distribution of outlet characteristics	43
Table 4: Survey weighted percentage of outlets with the outcomes	44-45
Table 5: Adjusted probability of outcomes in PRIVATE sector outlets	46
Table 6: Adjusted probability of outcomes in PUBLIC sector outlets	47
Table 7: Unweighted distribution of outlet characteristics	71
Table 8: Survey weighted means of continuous variables by outcomes	72
Table 9: Survey weighted mean <i>falciparum</i> malaria prevalence among outlet locations by pricing outcomes	73
Table 10a: Survey weighted percentages of outlets with the pricing outcomes	74
Table 10b: Survey weighted percentages of outlets with the pricing outcomes (for antimalarial stocking-related variables)	75
Table 11: Adjusted probability of stocking some co-paid QAACTs at RRP	76
Table 12: Adjusted probability of stocking all co-paid QAACTs at RRP	77
Table 13: Survey weighted relationship between number of co-paid QAACTs and proportion at RRP	78
Table 14: Unweighted distribution of sample characteristics	98
Table 15: Adjusted odds ratio of knowing the RRP for various outlet characteristics	99
Table 16a: Malaria epidemiologic zone, population, and number of cases per annum for public and private sector outlets within censused clusters	100
Table 16b: Malaria prevalence, population, and number of cases per annum for public and private sector outlets within censused clusters	101

List of Figures

Figure 1: Projected Effect of a Global Subsidy on ACT Prices	7
Figure 2: The AMFm Monitoring and Evaluation Results Framework	11
Figure 3: Conceptual Model	13

List of Appendices

Appendix A: Codebook for Appendices	122
Appendix B: Weighting	123
Appendix 1: Summary of AMFm outcomes in Ghana	124
Appendix 2: Map of Ecological Zones and Regions, Ghana 2011	125
Appendix 3: Output from the private sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 QAACT”, excluding the variable “Malaria testing (microscopy/RDT) available”, because it was not significant in the unadjusted analysis	126
Appendix 4: Output from the private sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 co-paid QAACT”, excluding the variable “Malaria testing (microscopy/RDT) available”, because it was not significant in the unadjusted analysis	127-128
Appendix 5: Output from the private sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 QAACT”, substituting the variable “Category of highest health-related qualification” (Cat3_healthqual) with “At least 1 employee is a pharmacist, nurse or doctor” (healthqualind)	129
Appendix 6: Output from the private sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 QAACT”, substituting the variable “Number of prescribers/dispensers employed” (Cat3_NoOfPrescribers) with “Number of employees” (Cat4_NoOfWorkers_auto)	130-131
Appendix 7: Output from the private sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 QAACT”, substituting variables “Category of highest health-related qualification” (Cat3_healthqual) and “Number of prescribers/dispensers employed” (Cat3_NoOfPrescribers) with “At least 1 employee is a pharmacist,	

nurse or doctor" (healthqualind) and "Number of employees" (Cat4_NoOfWorkers_auto) respectively	132
Appendix 8: Output from the public sector model showing the adjusted predictive power of training (trainedProg) for the outcome "stocked at least 1 QAACT", excluding the variable "Category of highest health-related qualification" (Cat3_healthqual)	133
Appendix 9: Output from the public sector model showing the adjusted predictive power of training (trainedProg) for the outcome "stocked at least 1 QAACT", excluding the variable "Category of highest health-related qualification" (Cat3_healthqual) and substituting the variable "Number of prescribers/dispensers employed" (Cat3_NoOfPrescribers) with "Number of employees" (Cat4_NoOfWorkers_auto)	134-135
Appendix 10: Discussion on the choice of proxies for outlet size	136-137
Appendix 11: Output from the model showing the adjusted predictive power of "Respondent knew and specified the RRP" (identRrp) for the outcome "At least 1 co-paid QAACTs sold at RRP" (AtleastqaactRRP) with inclusion of the variable "Stocked at least 1 non-QAACT" (outAmCat2)	138-139
Appendix 12: Output from the model showing the adjusted predictive power of "Respondent knew and specified the RRP" (identRrp) for the outcome "All co-paid QAACTs sold at RRP" (allqaactRRP) with inclusion of the variables "Stocked some oral AMTs" (outAmCat3_Oral), "Stocked some non-AMFm QAACTs" (outAmCat1_nologo), "Stocked some non-QAACTs" (outAmCat2), and "Stocked at least 1 nAT" (fixedoutAmCat4)	140-141
Appendix 13: Output from the model for the outcome "At least 1 co-paid QAACTs sold at <= 1 USD" (AtleastqaactRRP_oneUSD) instead of "At least 1 co- paid QAACTs sold at RRP" (AtleastqaactRRP)	142
Appendix 14: Output from the model for the outcome "All co-paid QAACTs sold at <= 1	

USD” (allqaactRRP_oneUSD) instead of “All co-paid QAACTs sold at RRP” (allqaactRRP)	143-144
Appendix 15: Distribution of actual price per treatment of adult does of co-paid QAACTs	145
Appendix 16 Graph showing the relationship between percentage of co-paid QAACTs at RRP and number of co-paid QAACTs per outlet	146
Appendix 17: Jitter plots showing the relationship between the predicted probability of (a) stocking at least 1 co-paid QAACT at RRP, (b) stocking all co-paid QAACT at RRP and malaria prevalence	147
Appendix 18: Distribution of outlets that had only 1 co-paid QAACT at RRP (a)	148
Appendix 19: Distribution of outlets that had only 1 co-paid QAACT at RRP (b)	149
Appendix 20: Mean, median (p50), and interquartile range prices per AETD of co-paid ASAQ and AL in our sample	150
Appendix 21: Predicted probabilities of knowing the RRP for various outlet Characteristics	151
Appendix 22: Adjusted Odds Ratios of Knowing the RRP for Selected Outlet Characteristics	152
Appendix 23: Output showing the marginal impact of training for rural outlets as increasing the probability of knowledge by 46% ($p<0.001$), while for urban outlets it was only 4.8% ($p=0.208$)	153
Appendix 24: Actual cases per outlet in malaria epidemiologic zones and prevalence Areas	154
Appendix 25: Percentage of the population living in censused “clusters” with outlets with QAACTs in stock at the time of survey, Ghana, 2011	155

List of Definitions and Abbreviations

Definitions

Antimalarial	Any medicine recognized by the WHO for the treatment of malaria. Medicines used solely for the prevention of malaria were excluded from analysis.
Artemisinin-based Combination Therapy (ACT)	An antimalarial that combines artemisinin or one of its derivatives with an antimalarial or antimalarials of a different class. Refer to Combination Therapy.
Artemisinin monotherapy (AMT)	An antimalarial medicine that has a single active compound, where this active compound is artemisinin or one of its derivatives.
Censused cluster	A cluster/sub-district where field teams conducted a full census of all outlets with the potential to sell antimalarials.
Cluster	<p>The primary sampling unit, or cluster, for the outlet survey. It is supposed to be an administrative unit typically determined by the Ministry of Health (MoH) that hosts a population size of approximately 10,000 to 15,000 inhabitants.</p> <p>In Ghana there is no existing intermediate administrative unit which is equivalent to a sub-district/cluster of 10,000-15,000 inhabitants. The smallest functional administrative units are the assemblies (district, municipal and metropolitan), which are subdivided into Enumeration Areas (EA) with average size of 750 inhabitants per each EA. Artificial sub-districts (clusters) were created by combining EAs for the purposes of the AMFm survey in Ghana.</p>
Combination therapy	The use of two or more classes of antimalarial drugs/molecules in the treatment of malaria that have independent modes of action.
Dosing/treatment regimen	The posology or timing and number of doses of an antimalarial used to treat malaria. This schedule often varies by patient weight.
Enumerated Outlets	Outlets that were visited by a member of one of the field teams, and where minimum basic descriptive information was collected
First-line treatment	The government recommended treatment for uncomplicated malaria. Ghana's first line treatment is Artesunate – Amodiaquine and the alternate first line treatment is Artemether – Lumefantrine.
Monotherapy	An antimalarial medicine that has a single mode of action. This may be a medicine with a single active compound or a synergistic combination of two compounds with related mechanisms of action.
Non-artemisinin therapy (nAT)	An antimalarial medicine that does not contain artemisinin or any of its derivatives.

Outlet	Any point of sale or provision of a commodity to an individual. Outlets are not restricted to stationary points of sale and may include mobile units or individuals. Refer to Appendix 9.6 for a description of the outlet types visited for this survey.
Quality Assured Artemisinin-Based Combination Therapies (QAACTs)	QAACTs are ACTs that comply with the Global Fund to Fight AIDS, Tuberculosis and Malaria's Quality Assurance Policy. For the purpose of the Independent Evaluation, a QAACT is any ACT which appeared on the Global Fund's indicative list of antimalarials meeting the Global Fund's quality assurance policy prior to baseline or endline data collection (see: http://www.theglobalfund.org/en/procurement/quality/pharmaceutical/#General), or which previously had C-status in an earlier Global Fund quality assurance policy and was used in a program supplying subsidized ACTs. At endline, QAACTs were defined as any ACT which appeared on the Global Fund's indicative list of antimalarials meeting its quality assurance policy as at September 2011, or which previously had C-status in an earlier Global Fund quality assurance policy and was used in a program supplying subsidized ACTs.
Screened	An outlet that was administered the screening questions of the outlet survey questionnaire (see Screening criteria).
Screening criteria	The set of requirements that must be satisfied before the full questionnaire is administered. In this survey, an outlet met the screening criteria if (1) they had antimalarials in stock at the time of the survey visit, or (2) they report having stocked them in the past three months.

List of Acronyms/Abbreviations

ACT	Artemisinin-based Combination Therapy
AL	Artemether-Lumefantrine
AMFm	Affordable Medicines Facility-malaria
ASAQ	Artesunate-Amodiaquine
BCC	Behavior Change Communication
CHPS	Community Health Planning Services
FDB	Food and Drugs Board
GHS	Ghana Health Services
Global Fund	The Global Fund to Fight AIDS, Tuberculosis and Malaria
GPS	Global Positioning System
IE	Independent Evaluation
IEC	Information Education & Communication
IRS	Indoor Residual Spraying

ITN	Insecticide-Treated Nets
LCS	Licensed Chemical Seller / Shop
LLITNs	Long Lasting Insecticide Treated Nets
MoH	Ministry of Health
NMCP	National Malaria Control Program
PPS	Probability Proportional to Size
QAACT	Quality Assured ACT
RBM	Roll Back Malaria
WHO	World Health Organization
SIVs	Supporting Interventions

Chapter 1: Specific Aims

The use of artemisinin-based combination therapies (ACTs), the most effective treatments for uncomplicated malaria, remains far below need. Reasons for low ACT uptake include: unreliable public sector supply; high prices and limited availability in the private sector, which is the most widely used source of treatment in many malaria endemic regions; and patient self-treatment with less expensive monotherapies. The Affordable Medicines Facility – malaria (AMFm), hosted by The Global Fund to Fight AIDS, Tuberculosis and Malaria, is a financing mechanism designed to increase affordability, availability, market share and use of quality assured artemisinin-based combination therapies (QAACTs). AMFm involves manufacturer price negotiations, factory gate price subsidies, and supporting interventions such as Information, Education and Communications (IE&C) campaigns.

Between 2010 and 2012, the AMFm was implemented in 8 pilots including Ghana, where its outcomes were independently evaluated. The AMFm Independent Evaluation (IE) was commissioned to gather evidence needed to inform decisions regarding the future of the AMFm. As part of the IE, national level baseline and endline outlet surveys were conducted involving the collection and analysis of primary data to answer three questions related to the availability, affordability and market share of quality-assured ACTs using a cluster sampling approach.

With a budget of up 450 million dollars and some uncertainty about its potential for success, AMFm was fraught with controversy, and provoked intense debate within the global health community on whether or not the program should be continued following the presentation of the IE findings to the Global Fund Board.

As some kind of "middle ground" stance, at the end of the 2-year pilot period of AMFm, in November 2012 the Global fund Board decided to integrate the AMFm into core Global Fund grant management and financial processes, following a transition period in 2013. In countries like Ghana, where the phase I pilot was shown to be highly successful, stakeholders were disappointed and angry with this decision, believing that the decision would reverse the gains made in availability and affordability of ACTs. The Global fund Board's decision further meant eligible countries would decide whether or not to allocate funding from their core Global Fund grants to subsidies for ACTs, and Ghana has already indicated that it will be moving in this direction.

Being a complex intervention, there are many aspects of the AMFm that can be researched. The purpose of this work is to contribute to the emerging body of knowledge on the outcomes of the AMFm in Ghana by exploring “*why*” and “*how*” the outcomes documented in the IE report came to be observed. The following specific aims are being pursued:

Specific Aims

1. In both the public and private sectors, to assess the differences in characteristics between outlets stocking QAACTs and those not having QAACTs in stock by exploring the relationship between having received training on co-paid QAACTs and stocking of QAACTs.
2. To further examine pricing of QAACT by determining how retailer's knowledge of the recommended retail price for QAACTs and other factors account for outlet's adherence to their recommended retail price in the private-for-profit sector.

3. To identify differences between urban and rural outlets in the impact of training on knowledge of the recommended retail price for co-paid QAACTs in private-for-profit outlets.

Findings from this project will shed light on the factors influencing the outcomes of the AMFm in Ghana and inform the implementation of subsequent interventions involving price subsidies on antimalarials and possibly other essential medicines in Ghana.

Chapter 2: Statement of Purpose and Background

Introduction

Malaria remains a leading parasitic cause of morbidity and mortality worldwide, accounting for almost one million deaths in 2011, 90% of which occurred in sub-Saharan Africa (WHO, 2012). The malaria-causing *Plasmodium* parasite is transmitted from human to human by the bite of the female *Anopheles* mosquito.

The entire Ghanaian population of 25 million lives at risk of malaria, and the disease accounts for 38.2% of all outpatient illnesses, 34.9% of all admissions, and 33.7% of all deaths in children under-five years (NMCP, 2010). The US Presidential Malaria Initiative (PMI) committed an amount of US\$ 26,100,000 to malaria control activities in Ghana for 2013 (PMI, 2013). Also, over the past decade Ghana has received over US\$ 150,000,000 to fund the prevention and treatment of malaria from the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) (The Global Fund, 2013).

A high level of coverage in use of effective antimalarials has been recognized as critical to the overall success of malaria control efforts globally (White et al., 1999). As such the Ghana National Malarial Control Program (NMCP) has included in its national strategic plan for malaria to, by 2015, be treating 90% of malaria patients in both public and private facilities with effective antimalarials (MoH, 2008).

Antimalarial policy and use

The World Health Organization (WHO) specifically recommends artemisinin-based combination therapies (ACTs) as first-line treatment for uncomplicated *P. falciparum* malaria¹ (WHO, 2006). Artesunate-Amodiaquine (ASAQ) was therefore

¹ Symptomatic infection with malaria caused by *Plasmodium falciparum* without evidence of vital organ dysfunction. *P. falciparum* is responsible for 98% of malaria infections in Africa.

selected by policy makers in Ghana as the first-line drug for uncomplicated malaria, following overwhelming evidence of widespread resistance to the previous first-line drugs, chloroquine and Sulphadoxine/Pyrimethamine (SP) (Driessen, Van Kerkhoven, Schouwenberg, Bonsu, & Verhave, 2002; Landgraf, Kollaritsch, Wiedermann, & Wernsdorfer, 1994; Trape et al., 1998). Artemether-Lumefantrine (AL) and Dihydroartemisinin-Piperaquine (DHAP) were later added as alternative first-line therapies for individuals who are intolerant to ASAQ (MoH, 2008). All the ACTs recommended in the national formulary have been declassified from prescription-only to over-the-counter medicines. ACTs can therefore be stocked, prescribed and supplied by all health providers, including practitioners in licensed retail medicine outlets like pharmacies and chemical shops (FDB, 2010).

Despite these efforts, ACTs account for only one in five anti-malarial treatments taken and are provided almost entirely by the public sector (The Global Fund, 2012a), through which the most part of developmental assistance for health is channeled (Adeyi & Atun, 2010). Over 60% of patients access anti-malarial treatment through the private sector, where ACTs make up only 5% of treatments provided (The Global Fund, 2012a). The relatively high prices and limited availability of ACTs particularly in rural areas, encourage treatment with other more common and much cheaper antimalarials, and has contributed to the low uptake of ACTs (O. J. Sabot et al., 2009). Making ACTs more available and lowering the price paid by the end user, could therefore be an effective way to increase their uptake (Arrow, Panosian, & Gelband, 2004; Moszynski, 2008).

The Affordable Medicines Facility - malaria

In 2002, the Board on Global Health of the Institute of Medicine (IOM) convened a committee to explore the economics of various treatment strategies for malaria. The committee published their report in 2004 advocating for a global subsidy on ACTs in both the public and private health sectors. This subsidy was to help ACTs outcompete older oral artemisinin monotherapies (AMTs)² and other cheaper and ineffective non-artemisinin therapies (nATs) on the market by making ACTs more available for use (Arrow et al., 2004).

Mathematical models comparing the introduction of a subsidy on ACTs with counterfactual scenarios, strongly supported the recommendations for a global subsidy on ACTs put forward by the IOM report (R. Laxminarayan, Over, & Smith, 2006). This idea of a global antimalarial subsidy received widespread international media attention, including features on the *BBC* and the *Voice of America* and in *The Lancet*, *British Medical Journal* and *Science* (Enserink, 2007; Samarasekera, 2008; Tanne, 2006).

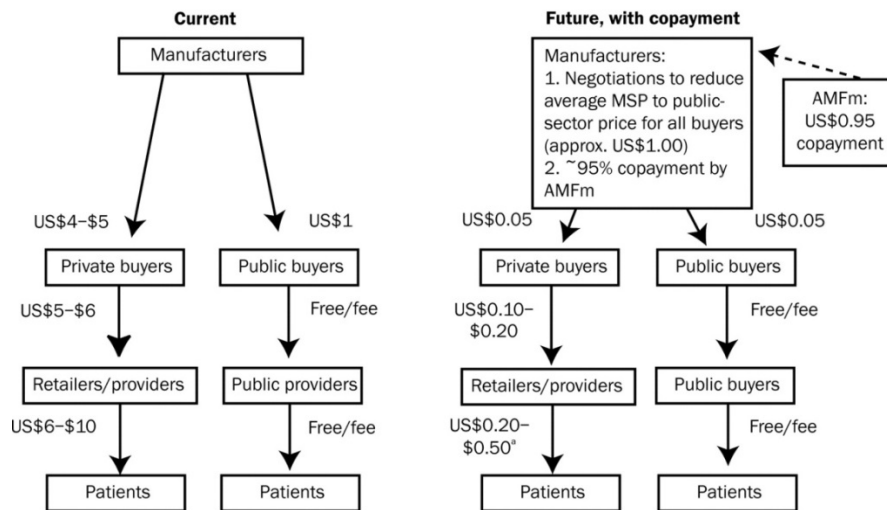
The Bill & Melinda Gates Foundation funded the Finance and Resources Working Group of the Roll Back Malaria (RBM) Partnership, chaired by the World Bank to draft a technical design for the operationalization of a global antimalarial subsidy. The subsidy was to facilitate access to ACTs by: 1) reducing prices through negotiations with manufacturers in order to reduce the maximum “factory gate”³ price of the ACTs; 2) providing a co-payment on ACTs that meet specific quality standards at the top of the global ACT supply chain on behalf of eligible first-line buyers from the public, private

² Persistent use of oral artemisinin monotherapies (AMTs) increases the risk of widespread parasite resistance to artemisinin, which remains the only widely effective first-line treatment.

³ The factory gate price is technically known as the ex-works price, and is the price of a drug at the manufacturer warehouse excluding all transportation and import/export costs.

for-profit and private not-for-profit health sectors; and 3) supporting various other interventions promoting the appropriate use of ACTs (see Figure 1) (Adeyi & Atun, 2010; RBM, 2007). This subsidy was to be administered by the Global Fund as a two-year pilot project in a selected number of countries, and was labeled the “*Affordable Medicines Facility – malaria phase I*” (AMFm).

Figure 1: Projected Effect of a Global Subsidy on ACT Prices



MSP: Manufacturer Sales Price; AMFm: Affordable Medicines Facility-malaria
Source: (Dalberg Global Development Advisors, 2007)

Implementation of the AMFm

Roll-out of the AMFm phase I was delayed till 2008, owing to key stakeholder’s uncertainty of the outcomes of this multidisciplinary complex health systems intervention (Ramanan Laxminarayan & Gelband, 2009). The AMFm Phase 1 pilot stated four objectives: 1) increased ACT affordability, 2) increased ACT availability, 3) increased ACT use, including among vulnerable groups, and 4) “crowding out” AMTs and nATs by gaining market share (The Global Fund, 2009b). The pilot cost approximately USD 463 million, and funding covering the amount was made available by the Bill & Melinda

Gates Foundation, the Governments of the United Kingdom and Canada, and UNITAID in addition to funds from the regular Global Fund grants to finance the supporting interventions at country level (Maxmen, 2012a; The Global Fund, 2008).

Ghana was among eight countries successful in securing AMFm Phase I funding (Ghana CCM, 2009). Following Ghana's approval, eligible wholesalers known as first-line buyers (FLBs), signed contracts with the Global Fund and placed orders for the co-paid ACTs with eligible manufacturers (The Global Fund, 2009b). Of the 32 Ghanaian FLBs who registered with the Global Fund, only 14 private sector FLBs and the MoH were able to place orders for co-paid ACTs, because manufacturers preferred working with FLBs with whom they had previous experience as local distributors or agents (AMFm IE Team, 2012). ACTs that were eligible for Global Fund co-pays had to be approved by the WHO Prequalification Programme (The Global Fund, 2010) and were referred to as Quality Assured ACTs (QAACTs).

On September 02, 2010, the first co-paid QAACTs entered the Ghanaian private sector supply chain, and although scheduled to have begun earlier, Information Education & Communication (IEC) as well as Behavior Change Communication (BCC) activities commenced within that same month (J. Amuasi, Nguah, Diap, Ansong, & The Independent Evaluation Team, 2012).

The AMFm Independent Evaluation and its limitations

Although several smaller studies had been carried out to ascertain the impact that price subsidies and other related interventions could have on availability and price of antimalarials (Yamey, Schäferhoff, & Montagu, 2012), the AMFm was the first ever

large scale implementation of a subsidy scheme on medicines (Bump, Fan, Lanthorn, & Yavuz, 2012).

The Global Fund developed a multi-faceted monitoring and evaluation framework for the AMFm Phase I. A key component of this framework was an Independent Evaluation (IE) to assess how AMFm played out in each pilot country. An Independent Evaluation team was contracted to conduct and measure changes between baseline and endline surveys in availability, price, market share and use of quality-assured ACTs (QAACTs). Evidence from the IE was to inform the Global Fund Board's decision regarding the future of AMFm after the Phase I period (The Global Fund, 2009a).

The IE was based on a non-experimental design, with pre- and post-test intervention assessment of key indicators and measurement of changes for rural and urban domains. Tougher et al describe the data collection and analysis process (Tougher et al., 2012). In Ghana the baseline survey took place in August 2010, and the endline survey took place in November 2011 (J. Amuasi et al., 2012).

The IE of AMFm phase I was focused on outputs and outcomes, although some effort was made to contextualize these by analysis of qualitative information on the AMFm implementation process in each country (The Global Fund, 2009a; Willey et al., 2014). Nevertheless, apart from measuring changes in key indicators pre- and post-intervention, an analysis of some aspects of the process; “*how*” and “*why*” the changes observed took place is lacking, and is critical to determining implementation failure, genuine ineffectiveness of an intervention or the best way forward (Craig et al., 2008; de Savigny & Adam, 2009; Habicht, Victora, & Vaughan, 1999).

Purpose of the Dissertation

The gaps in understanding the AMFm and how it impacted the countries where it was piloted, allow several opportunities for further research. The ongoing interest in the AMFm and its incorporation into the core Global Fund grant management and financial processes means subsidies for antimalarial drugs will remain a subject of attention for the foreseeable future. In this regard additional understandings of the dynamics of the AMFm intervention are needed.

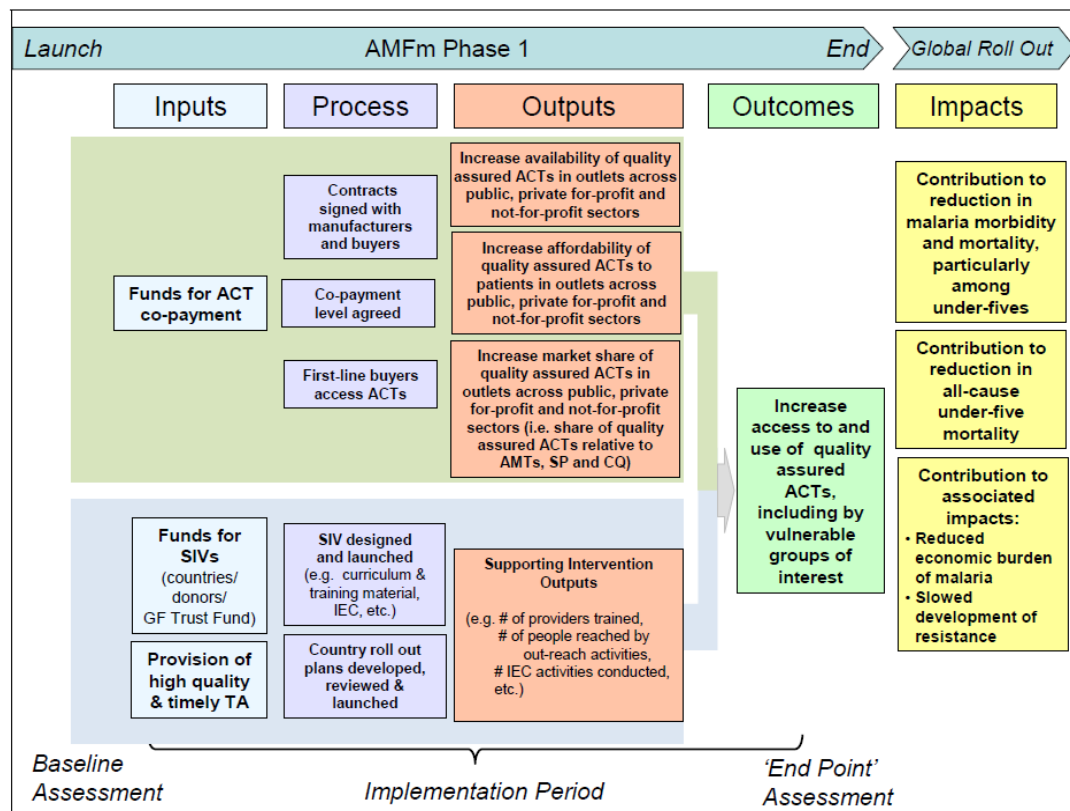
This dissertation aims to improve understanding of “*how*” and “*why*” the AMFm had the impact it did in Ghana as elaborated in the IE report by: 1) exploring the relationship between various outlet characteristics and QAACT stocking in both the public and private sector; 2) further examining QAACT pricing by determining factors accounting for outlet’s adherence to their recommended retail price in the private-for-profit sector; and 3) identifying differences between urban and rural outlets in the impact of training on knowledge of the recommended retail price for co-paid QAACTs in private-for-profit outlets. The malaria control policy implications of our findings are also discussed.

Theory and Conceptual Model

The AMFm IE identified increases in availability, affordability, market share and use of QAACTs as the desired outputs, and increase in access to and use of QAACTs as desired outcomes of the AMFm Phase I, as shown in Figure 2 (The Global Fund, 2009a). While these labels are appropriate, based on the pre-test and post-test intervention assessment design of the IE, the naïve reader may get the impression that the outputs and

by extension outcomes are “stacked on each other” or occur simultaneously. However, careful examination of these outputs/outcomes, as well as inputs (funds for ACT co-payment and SIs) and processes (FLBs access to ACTs, country roll out of SIs etc.) reveals important relationships that can be examined to better explain *why* the observed outputs and outcomes.

Figure 2: The AMFm (Phase 1) Monitoring and Evaluation Results Framework



ACTs: Artemisinin-based combination therapies; IEC: Information Education and Communication; GF: Global Fund, AMTs: Antimalarial Treatment; SP: Sulfadoxine-pyrimethamine, CQ: Chloroquine; TA: Technical Assistance, SIVs: Supporting Interventions

Source: (The Global Fund, 2009a)

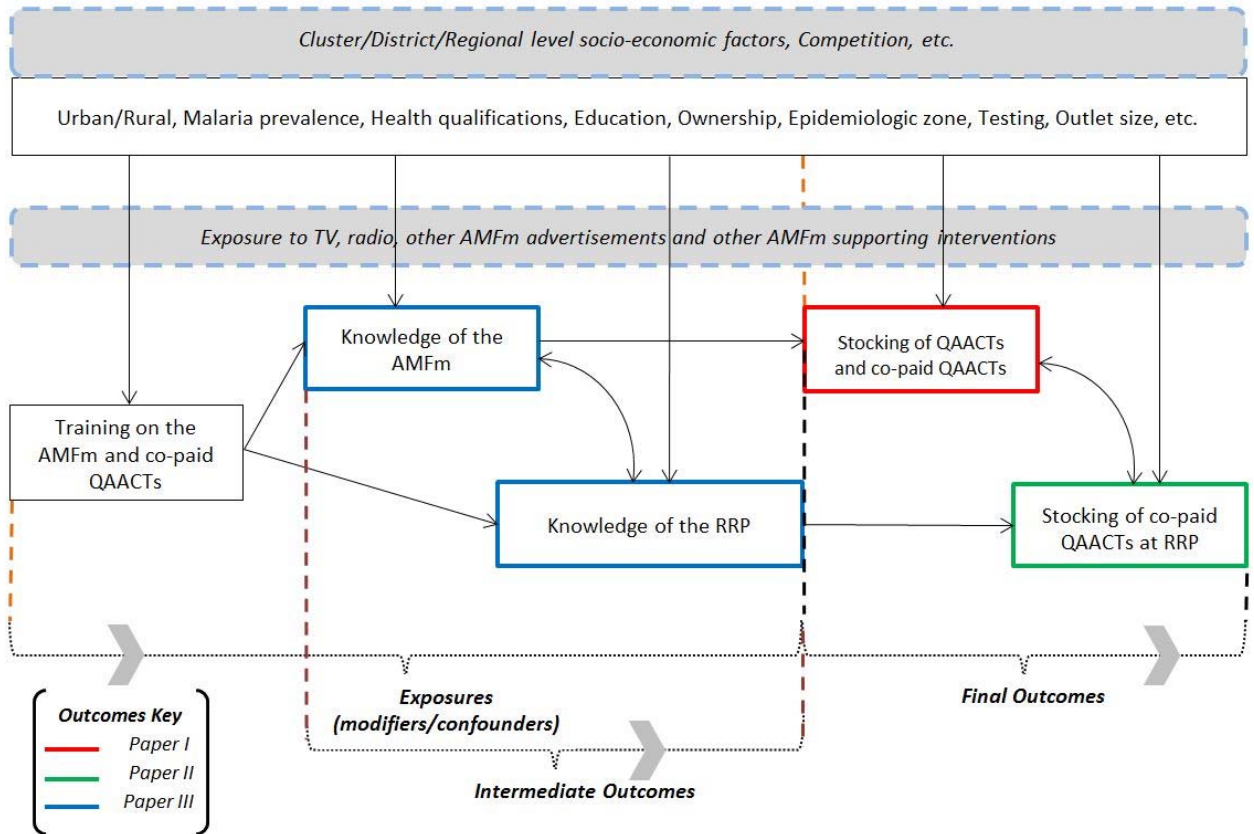
The conceptual model shown in Figure 3 depicts our hypothesized relationship between training and knowledge of the AMFm intervention and of the recommended retail price for the co-paid QAACTs. An important product/intermediary outcome of the country roll out of SIVs, particularly training of retailers, prescribers and dispensers, was

the creation of knowledge about the AMFm intervention and the recommended retail price (RRP) for QAACTs. FLBs needed to actively seek out contracts with manufacturers, and outlets in turn needed to purchase from FLBs for retail to consumers. Thus, knowledge about the AMFm intervention was cardinal to achieving widespread availability of QAACTs. Knowledge is further hypothesized as being directly related to stocking of QAACTs and stocking of co-paid QAACTs at the RRP.

Stopping at this linear description of relationships would be overly simplistic, as there are several potential influencing factors/characteristics and interrelationships among them. As such we hypothesize that a number of geographic, socio-economic, malaria epidemiologic and other factors are also related to training, knowledge of the AMFm/RRP and stocking of QAACTs.

The conceptual model is however limited to depicting only the relationships of interest and relevance to antimalarial policy in Ghana and mainly those which are measurable using the data available from the IE and other secondary sources.

Figure 3: Conceptual Model



Note: The variables in the dashed blue boxes are not measurable from the data available.

The data set

Data from the AMFm Phase I independent evaluation endline survey in Ghana was used as the primary source of data used to achieve the aims outlined in this dissertation. The data collection, analysis process and findings of the IE endline survey are described in other sources (J. Amuasi et al., 2012; Tougher et al., 2012; Willey et al., 2014). Shapefiles and other geographic information systems data on districts in Ghana were obtained from the Centre for Remote Sensing and Geographic Information Services of the University of Ghana via ESRI's GeoCommons platform (CERSGIS, 2012). Data on *Plasmodium falciparum* malaria prevalence by district were obtained from the 2010

posterior predictive distribution model estimates produced by the Malaria Atlas Project (MAP). Further details on the MAP methodology are available from other publications (Gething et al., 2011; MAP, 2010).

The IE endline survey data comprise information on 1,093 outlets and 7,389 antimalarial products. We however excluded outlets which were not screened (n=91), did not meet the screening criteria (n=28), were not interviewed (n=6), did not fully complete the interview and antimalarial audit (n=3), a community health worker (n=1), and those that were private not-for-profit facilities (n=13) from the dataset.

Antimalarials were divided into four broad categories; non-artemisinin therapies (nAT), artemisinin monotherapies (AMT), antimalarials no longer used for treatment but only for prophylaxis (nRx), and artemisinin-based combination therapy (ACT). nATs were classified into Sulphadoxine-pyrimethamine (SP - WHO recommended for intermittent preventive therapy in pregnancy [IPTp]), quinine (used for treating severe malaria), and other nATs. AMTs were classified into oral and non-oral AMTs. ACTs were subdivided into quality-assured ACTs (QAACTs) and non-quality-assured ACTs, and QAACTs were further classified based on whether or not the AMFm green-leaf logo was present on the packaging. The presence of the logo on a product's packaging was used to identify those QAACTs which were subsidized by AMFm.

The data used for this dissertation, including variables, is described in Table 1 below.

Table 1: Distribution of outlet and respondent characteristics in AMFm IE dataset

Characteristics		*Type of outlet, n or N (%)		
		<i>Public</i> <i>n = 303</i> <i>(31.9)</i>	<i>Private</i> <i>n = 648</i> <i>(68.1)</i>	<i>All</i> <i>N = 951</i> <i>(100)</i>
Stocked an antimalarial		298 (98.4)	642 (99.1)	940 (98.8)
Stocked at least 1 QAACT		242 (79.9)	563 (86.9)	805 (84.7)
Stocked at least 1 co-paid QAACT		228 (75.3)	545 (84.1)	773 (81.3)
Stocked at least 1 SP or Quinine		175 (57.8)	436 (67.3)	611 (64.3)
Stocked at least 1 oral AMT		5 (1.7)	348 (53.7)	353 (37.1)
Stocked at least 1 nAT**		9 (3)	343 (52.9)	352 (37)
Stocked at least 1 antimalarial used for prophylaxis or no longer used for treatment		0	19 (2.9)	19 (2)
Stocked at least 1 co-paid QAACTs without stocking any AMTs or nATs**		215 (71)	130 (20.1)	345 (36.2)
Malaria testing (microscopy/RDT) available		121 (39.9)	29 (4.5)	150 (15.8)
At least 1 employee was a nurse, pharmacists or doctor		256 (89.8)	333 (53.5)	589 (65)
At least 1 employee had a health-related qualification		281 (98.6)	435 (70.6)	716 (79.5)
At least 1 employee had completed secondary/high school		293 (96.7)	598 (92.3)	891 (93.7)
At least 1 employee received training on QAACTs with the logo		178 (58.8)	298 (46)	476 (50.1)
Respondent owned the outlet		-	237 (36.6)	237 (24.9)
Respondent correctly stated the recommended first-line antimalarial		294 (97)	566 (87.5)	860 (90.5)
Respondent correctly stated the max. RRP for co-paid QAACTs		262 (95.3)	535 (94)	797 (94.4)
Respondent had heard about the AMFm intervention		263 (86.8)	499 (77)	762 (80.1)
Respondent was able to recognize the AMFm logo		292 (96.4)	609 (94.4)	901 (94.7)
Location	<i>Urban</i>	95 (31.4)	474 (73.2)	569 (59.8)
	<i>Rural</i>	208 (68.7)	174 (26.9)	381 (40.2)
Malaria epidemiologic zone [§]	<i>Coastal savanna/Mangrove swamps</i>	73 (24.1)	310 (47.9)	383 (40.3)
	<i>Tropical rain forest</i>	151 (49.8)	247 (38.1)	398 (41.9)
	<i>Northern savanna</i>	79 (26.1)	91 (14)	170 (17.9)
Number of prescribers/dispensers employed	<i>1 - 2</i>	141 (46.5)	381 (58.8)	522 (54.9)
	<i>3 - 4</i>	103 (34)	210 (32.4)	313 (32.9)
	<i>5 or more</i>	57 (18.8)	53 (8.2)	110 (11.6)
Survey weighted mean number of prescribers/dispensers employed (95% CI)		3.4 (3.1, 3.7)	2.6 (2.5, 2.7)	2.8 (2.7, 3)
Survey weighted mean number of antimalarials audited (95% CI)		4 (3.8, 4.3)	9.5 (9, 10)	7.7 (7.4, 8.2)

*Percentages may not total 100 because of rounding or missing data

**Excludes SP, Quinine, and those antimalarials used strictly for prophylaxis or no longer for treatment

[§]Approximation based on demarcations of ecological zones (Coastal, Forest and Savanna) used by the Ghana Statistical Service

Importance of the dissertation to malaria research

Right from its inception, the idea of a subsidy on antimalarials was subjected to intense debate among powerful stakeholders with differing opinions as to its feasibility and potential outcomes (A. Talisuna et al., 2009). The major concerns of opponents of the subsidy included the safety of widespread distribution of ACTs based on clinical diagnosis only, particularly in the private sector; and the cost-effectiveness of the AMFm relative to other malaria interventions. Therefore the final consensus to pilot the subsidy for 2 years as AMFm Phase I was reached with considerable effort from proponents of the subsidy (Ramanan Laxminarayan & Gelband, 2009; The Lancet, 2009).

Even after the AMFm was launched, the debate on its viability continued (Adeyi & Atun, 2009; Bate, Milligan, & Mooney, 2012; Moon, Pérez Casas, Kindermans, de Smet, & von Schoen-Angerer, 2009; O. Sabot, Gordon, Moonen, Talisuna, & Amofah, 2011; Siva, 2009). Critics continued to voice their opposition to the program (Bate & Hess, 2009; Kamal-Yanni, 2010), including challenging the approaches to measurement of the program's effectiveness (Tren & Hess, 2011). Thus, before the Global Fund Board met to decide on what to do with AMFm (continue, amend or terminate), there was a renewed frenzy of debate on the subject (Maxmen, 2012a, 2012b), with critics tendering in what they believed was evidence justifying their concerns about the AMF intervention (Bate, Hess, et al., 2012; Kamal-Yanni, 2012). Supporters of the intervention were concerned that it would be terminated, despite what they touted as evidence from the independent evaluation that benchmarks of success had largely been achieved (Ramanan Laxminarayan, Arrow, Jamison, & Bloom, 2012).

As some sort of "middle ground" stance, at the end of the 2-year pilot period of the AMFm, in November 2012, the Global Fund Board decided to integrate the AMFm into core Global Fund grant management and financial processes, following a transition period in 2013 (The Global Fund, 2012b). This decision meant eligible countries would decide whether or not to allocate funding from their core Global Fund grants to subsidies for ACTs. Proponents of the AMFm were disappointed given what they believed was evidence of the success of the AMFm Phase I (Bump et al., 2012). Authors of the 2004 IOM report that proposed the idea of a global subsidy on antimalarials labeled the decision as “effectively killing the AMFm program”, because countries Global Fund budgets are already committed to public sector priorities, and reallocating some of this to include private sector support would be most unlikely (Arrow et al., 2012).

In countries like Ghana, where the phase I pilot was shown to be highly successful, stakeholders were concerned about the uncertainty that shrouded the AMFm Phase I as to its continuation or otherwise (Maxmen, 2012b; A. O. Talisuna et al., 2012). Thus, many were disappointed and angry with the Global Fund’s decision, believing that it would reverse the gains made in availability and affordability of ACTs. Concerns have also been raised about the implications the Global Fund Board’s decision has for the global supply of raw materials for ACTs, especially artemisinin (Shretta & Yadav, 2012). However, it is not clear as yet if the “final chapter in the AMFm’s story” has yet been written (Ramanan Laxminarayan & Gelband, 2009), as it depends on how countries respond to the new financing arrangement put forward by the Global Fund.

This dissertation sheds light on some of what accounted for the findings of the AMFm IE in Ghana. It is critical to informing malaria policy and its implementation for

optimal outcomes. Some AMFm phase I countries including, Ghana, have expressed willingness to voluntarily commit some of their Global Fund allocation and other resources to antimalarial drug subsidies after the AMFm. Thus, knowing the critical components of success of the AMFm, and the pitfalls to avoid, is useful for the future design of further interventions involving subsidies for medicines and diagnostics.

Chapter 3: The AMFm in Ghana: Exploring Training and other Factors as Predictors of Stocking Practices

Introduction

The Affordable Medicines Facility-malaria (AMFm) phase 1 sought to increase the availability of quality-assured artemisinin-based combination therapies (QAACTs) in public and private health sector outlets. We examine the association between outlet and other characteristics and availability in public and private health sector outlets in Ghana following the AMFm intervention.

We used data collected as part of the AMFm Independent Evaluation endline survey in Ghana. We used chi-square analyses and logistic regression to generate the predicted probability of whether an outlet had QAACTs available defined in three different ways: i) Stocked at least 1 QAACT, ii) Stocked at least 1 co-paid QAACT, and iii) Stocked at least 1 co-paid QAACT without stocking any oral artemisinin monotherapies or non-artemisinin therapies. Variables in the model included participation in training, education and health-related qualification, number of prescribers, availability of testing, rural/urban status and malaria epidemiologic zone.

Factors associated with QAACT availability in the 951 (31.9% public and 68.1% private sector) outlets included in our study differed between and within public and private sectors for the various QAACT availability definitions. While a high percentage of public (75.3%) and private (84.1%) outlets stocked at least 1 co-paid QAACT, there was a large disparity (71% vs. 20.1%) between the two sectors when not stocking artesunate monotherapies (AMTs) and non-artemisinin therapies (nATs) was included in the definition of QAACT availability. In the private sector, having received training was

associated with a high predicted probability of stocking at least 1 QAACT (85.2%, $p=0.039$) and stocking at least 1 co-paid QAACT (84.9%, $p=0.020$), but not with stocking co-paid QAACTs without stocking any AMTs or nATs” (22.9%, $p=0.171$). However in the public sector, training was not a statistically significant predictor of any definition of QAACT availability.

Although high QAACT availability was achieved post the AMFm across public and private sector antimalarial markets in Ghana, predictors of antimalarial stocking vary considerably between the two sectors. The centralized nature of public sector commodity procurement and service delivery mechanisms makes it simpler to achieve adherence to antimalarial policy with respect to not stocking AMTs and nATs. The larger more complicated nature of the private sector antimalarial market makes it more difficult for it to be regulated, monitored and aligned with national policy. In-service training is generally an important tool towards improving QAACT stocking practices especially in the private sector. However, getting outlets to hire staff with health-related qualifications should be pursued as an effective long-term approach towards achieving ACT stocking benchmarks and recommended treatment practice.

Background

The entire Ghanaian population of over 25 million lives at risk of malaria, and transmission in Ghana occurs throughout the whole year with a slight increase during the rainy season (MoH, 2008, 2009b; NMCP, 2010). Data from mainly government health facilities shows that malaria accounts for 38.2% of all outpatient illnesses, 34.9% of all admissions, and 34% of all deaths in children under 5 years in Ghana (NMCP, 2010). As

with other malaria-endemic countries, these estimates of malaria burden may account for a small fraction of actual malaria infections, since a significant number may present for treatment in the private sector, particularly pharmacies and licensed chemical shops (Adeyi & Atun, 2010; J G Breman, 2001; Buabeng, Matowe, Smith, Duwiejua, & Enlund, 2010; PMI, 2011).

Owing to widespread resistance to chloroquine and other long-serving antimalarials (Driessen et al., 2002; Landgraf et al., 1994; Trape et al., 1998), the World Health Organization (WHO) has specifically recommended artemisinin-based combination therapies (ACTs) as first-line treatment for uncomplicated *P. falciparum* malaria (WHO, 2006). The overall success of malaria control efforts in reducing morbidity and mortality from the disease depends in part on a high level of availability and use of these highly effective ACTs (Bhattarai et al., 2007; Otten et al., 2009). However, use of ACTs in several malaria endemic countries including Ghana has remained chronically low (Flegg et al., 2013), significantly below the levels needed to achieve favorable health outcomes (WHO, 2010b).

Public and private sector outlets in many malaria endemic countries in sub-Saharan Africa play complementary roles in providing access to antimalarial treatment (Littrell et al., 2011; O'Meara, Obala, Thirumurthy, & Khwa-Otsyula, 2013; Williams & Jones, 2004). However the two sectors function in different and complex ways, resulting in different kinds of challenges with regard to availability and accessibility of ACTs. For example it was reported both in East and West African countries that in the public sector, although outlets stocked ACTs, low uptake resulted more from frequent stock-outs. In contrast, private sector outlets hardly stocked any ACTs, and those that did, sold them at

much higher prices than other less effective antimalarials (J. H. Amuasi et al., 2012; J. Amuasi, Diap, et al., 2011; B. B. Kangwana et al., 2009; Zurovac et al., 2008). Yet in several malaria endemic countries, over 60% of malaria patients have no option other than to obtain their antimalarials via the private sector because of poor access to public sector facilities (Cohen et al., 2010; Goodman, Kachur, Abdulla, Bloland, & Mills, 2009; Littrell et al., 2011; The Global Fund, 2012a). Thus the high prices of ACTs in the private sector left them unaffordable to those who need them the most (Arrow et al., 2004; Cohen et al., 2010; Patouillard, Hanson, & Goodman, 2010; O. J. Sabot et al., 2009; A. Talisuna et al., 2009).

In 2004, a committee convened by the US Institute of Medicine (IOM) published a report advocating for a global subsidy on ACTs in both the public and private health sectors (Arrow et al., 2004). This was even though traditionally, most developmental assistance for health has been channeled through the public sector (Adeyi & Atun, 2010). It was argued that a global subsidy on ACTs would help them outcompete other cheaper and ineffective antimalarials on the market by making ACTs more available and affordable (Arrow et al., 2004). Following intense debate on the feasibility of its implementation and expected outcomes (Ramanan Laxminarayan & Gelband, 2009), the Affordable Medicines Facility – malaria (AMFm) was initiated in 2008, administered by a dedicated secretariat at the Global Fund (Adeyi & Atun, 2010). The intervention was aimed at influencing markets, and did not involve any change in malaria treatment policies.

The AMFm comprised: 1) price reductions through negotiations with manufacturers of ACTs; 2) providing a co-payment on behalf of eligible wholesalers

known as first-line buyers (FLBs), for ACTs that met specific quality standards; and 3) supporting interventions (SIVs) promoting the appropriate use of ACTs (Adeyi & Atun, 2010). SIVs included training of prescribers/dispensers on how to treat uncomplicated malaria using existing policy-recommended ACTs with a focus on co-paid QAACTs. For easy identification, the Global Fund designed a logo depicting a green leaf (referred to as the “AMFm Logo”), which manufacturers with orders from FLBs printed on the packages and blisters they produced. ACTs that were eligible for purchase with Global Fund resources as part of the AMFm intervention had to be prequalified by the WHO Prequalification Programme (The Global Fund, 2010) and were referred to as Quality Assured ACTs (QAACTs).

Making QAACTs widely available and removing non-ACTs from the market is a key policy goal of market-based malaria control interventions like the AMFm (Adeyi & Atun, 2009). The AMFm was designed to run as a two-year pilot project known as the “AMFm Phase I” in Ghana, Kenya, Madagascar, Niger, Nigeria, Uganda, and Tanzania (mainland and Zanzibar). The AMFm Phase 1 pilot had four objectives: 1) increased ACT affordability, 2) increased ACT availability, 3) increased ACT use, including among vulnerable groups, and 4) “crowding out” oral artemisinin monotherapies, chloroquine and sulfadoxine-pyrimethamine (SP) by gaining market share (The Global Fund, 2009b).

The Global Fund initiated a multi-faceted monitoring and evaluation framework for the AMFm Phase I. A key component of this framework was an Independent Evaluation (IE) in each pilot country. The Independent Evaluation (IE) team was therefore commissioned to assess the achievement of the AMFm objectives by measuring

changes between baseline and endline surveys in availability, price, market share and use of QAACTs (AMFm IE Team, 2012; The Global Fund, 2009a). In Ghana the AMFm IE was national in scale, covering the country's ten regions. The AMFm IE in Ghana showed that the promotion of the AMFm led to a high provider awareness of the intervention, logo, and recommended retail price (RRP) at endline (J. Amuasi et al., 2012). Correspondingly, QAACT availability across all outlets in Ghana increased by 52 percentage points, from 31% at baseline to 83% at endline ($p<0.0001$) (AMFm IE Team, 2012; Tougher et al., 2012). See Appendix 1 for a summary of the AMFm outcomes in Ghana.

This paper examines public and private sector outlet characteristics and how these characteristics are able to predict outlets that did and those that did not have QAACTs in stock.

Methods

Data source

We used data collected as part of the AMFm IE endline survey in Ghana. The IE used a non-experimental design with pre- and post-test intervention assessment of key indicators and measurement of changes for rural and urban domains. A cluster sampling approach was adopted with a predetermined number of geographic clusters selected with probability proportional to size. Other sources describe the IE data collection and analysis process in detail (J. Amuasi et al., 2012; Tougher et al., 2012). In Ghana the endline survey took place from November 7–28, 2011, 15 months after the baseline survey (J. Amuasi et al., 2012). Ethical clearance for the IE surveys in Ghana was obtained from the

Ghana Health Service Ethical Review Committee on Research Involving Human Subjects (ERCRIHS). The University of Minnesota Institutional Review Board (IRB) further determined that our study was using secondary data, did not meet the regulatory definition of research with human subjects, and so did not require IRB clearance.

Data management

The IE endline survey data comprise information on 1,093 outlets and 7,389 antimalarial products. In our study, we included outlets that were enumerated and completed the interview regardless of whether or not they stocked antimalarials. Excluded from the sample were those outlets which were not screened, did not meet the screening criteria, were not interviewed, did not fully complete the interview and antimalarial audit, a community health worker, and those that were private not-for-profit facilities.

We divided antimalarials into four broad categories; non-artemisinin therapies (nAT), artemisinin monotherapies (AMT), antimalarials no longer used for treatment but only for prophylaxis (nRx), and artemisinin-based combination therapy (ACT). nATs were classified into Sulphadoxine-pyrimethamine (SP - recommended by the WHO for intermittent preventive therapy in pregnancy [IPTp]), quinine (used for treating severe malaria), and other nATs. AMTs were classified into oral and non-oral AMTs. ACTs were subdivided into quality-assured ACTs (QAACTs) and non-quality-assured ACTs, and QAACTs were further classified based on whether or not the AMFm green-leaf logo was present on the packaging. The presence of the logo on a product's packaging was used to identify those QAACTs which were subsidized by AMFm.

Variables

We measured QAACT availability in an outlet, in three different ways: i) The outlet “stocked at least 1 QAACT” (yes/no), ii) it “stocked at least 1 co-paid QAACT” (yes/no), and iii) it “stocked at least 1 co-paid QAACT without stocking any AMTs or nATs”, excluding those used strictly for prophylaxis, SP, and quinine, (yes/no). Having an employee who attended a training session on co-paid QAACTs was selected as the main potential independent predictor of QAACT availability. Ghana can be stratified into three main malaria epidemiologic zones: i) the northern savanna, ii) the tropical rainforest, and iii) the coastal savanna and mangrove swamps (GSS, 2011; MoH, 2009b) (see Appendix 2). We also evaluated the association between QAACT availability and other outlet-level characteristics, such as location features (malaria epidemiologic zone, rural/urban designation), availability of diagnostic testing, outlet size, and education level of outlet staff (see Table 2).

Statistical approach

The AMFm was the first major market-based intervention whose scope included the private sector along with the public sector. Although interconnected and complementary, the fundamental differences in characteristics and operations between the public and private antimalarial markets in Ghana alluded to earlier, led us to stratify all analyses by public and private sector.

For all analyses, we used the IE endline survey weights to account for the complex survey design used. We used chi-squared tests to assess the unadjusted relationship between our three definitions of QAACT availability and the independent variables listed in Table 2. We followed with multivariate logistic regression and post-

estimation techniques to determine the predicted probability of our three outcome definitions of QAACT availability. We adjusted for training, urban/rural status, and only those other variables that were statistically significant from our examination of the unadjusted relationships between independent variables and the outcomes. Thus, different models were specified for public and private sector outlets. Certain variables were excluded from consideration *a priori*. For example, the variable “respondent owned outlet” (yes/no) was not applicable in the model specified for the public sector. In all models, we performed sensitivity analyses to ensure that the observed effects were not an artifact of our modeling decisions (see Appendices 3 - 9). All analyses were carried out using STATA v12 and *p*-values were 2-sided with a level of significance of ≤ 0.05 .

Results

Outlet characteristics

From the AMFm IE dataset, we identified 951 outlets (87% of the IE dataset) that were enumerated and completed the interview; 31.9% were public sector outlets and 68.1% were private sector outlets. Table 3 shows the distribution of the characteristics of the outlets included in this study. For public sector outlets, the majority were from rural areas (68.7%), whereas the opposite was true for private sector outlets, where 73.2% were from urban areas. With respect to malaria epidemiologic zones, half of public sector outlets were from the forest zone (49.8%), while the remaining half was equally distributed between the coastal (24.1%) and savanna (26.1%) zones. On the other hand, almost half of private sector outlets were from the coastal zone (47.9%) and 38.1% and 14% were from the forest and savanna zones respectively. Hardly any outlets from the

private sector offered any kind of malaria testing (4.5%), whereas over one-third of outlets from the public sector had malaria testing available (39.9%).

Table 4 shows the distribution of variables and survey weighted percentage of outlets with the three outcomes in public and private for-profit outlets. Without adjusting for other covariates, consistently, the proportion of outlets for all three outcome definitions was higher among urban outlets in the private sector, and *vice versa* in the public sector. The rural/urban location of the outlet had a relationship with stocking QAACTs and stocking co-paid QAACTs among private sector outlets only ($p=0.026$ and $p=0.015$ respectively). Also without adjusting for other covariates, malaria epidemiologic zone was associated with all the outcome definitions across both public and private sector outlets except with stocking “at least 1 co-paid QAACT without stocking any AMTs or nATs” in the private sector ($p=0.153$). However the proportion of outlets with the outcomes did not follow a consistent pattern across malaria epidemiologic zones and/or outcome definitions. Availability of malaria testing was positively associated with only stocking “at least 1 co-paid QAACT without stocking any AMTs or nATs” in the private sector in our analysis without adjusting for other covariates. For private sector outlets, 36.6% of the survey respondents were the owners. We were concerned that owners might be more inclined to withhold information they might consider as casting their outlet in bad light. However there was no relationship between the interviewee’s ownership status and any of the outcome definitions.

In the private sector, a high number of outlets (92.3%) had at least one member of staff who had completed secondary/high school, which was positively associated with stocking at least 1 QAACT ($p<0.001$) and stocking at least 1 co-paid QAACT ($p<0.001$).

In outlets from the public sector, 84.5% had at least 1 member of staff who was formally trained and certified to prescribe or dispense medications (a nurse/midwife, pharmacist/dispensing technician or medical doctor/medical assistant); only 51.4% of outlets from the private sector had the same. Category of health-related qualification was positively associated with all the outcome definitions in only the private sector.

Almost half (46.5%) of the outlets from the public sector and over half (58.8%) of private sector outlets had 1-2 prescribers/dispensers, while 34% and 32.4% of public and private sector outlets respectively had 3-4 prescribers. Only 8.2% (53) of outlets from the private sector had 5 or more prescribers. All these larger outlets had at least 1 QAACT in stock, and 52 out of 53 had at least 1 co-paid QAACT in stock. The category of number of prescribers was positively associated with all the outcome definitions in both sectors except with respect to stocking “at least 1 co-paid QAACT without stocking any AMTs or nATs” in the public sector. At 3.6 (95% CI: 3.1 – 4), the survey weighted mean number of prescribers/dispensers per outlet was higher in the public sector than in the private sector at 2.2 (95% CI: 2.1 – 2.4).

Training and antimalarial stocking practices

Almost half (46%) of private sector outlets had at least one member of staff who had received training on the AMFm intervention, while 58.8% of public sector outlets had the same. Without adjusting for other covariates, training was a significant predictor of stocking at least 1 QAACT and stocking at least 1 co-paid QAACT in only the private sector ($p=0.032$ and $p=0.020$ respectively).

With respect to achieving the three QAACT availability outcomes, the percentage of outlets in both public and private sectors decreased with increasing level of complexity

of the outcome definition: In the public sector, 79.9% stocked at least 1 QAACT; 75.3% stocked at least 1 co-paid QAACT; and 71% stocked at least 1 co-paid QAACT without stocking any AMTs or nATs. A similar trend is seen in the private sector, with 86.9% of outlets stocking at least 1 QAACT; 84.1% stocking at least 1 co-paid QAACT; and a precipitous drop to 20.1% of outlets stocking at least 1 co-paid QAACT without stocking any AMTs or nATs. While only 1.7% and 3% public sector outlets stocked the non-policy recommended AMTs and nATs respectively, disappointingly, 53.7% and 52.9% respectively of private sector outlets stocked AMTs and nATs.

Predicted probability of stocking QAACTs after adjusting for other covariates

Tables 5 and 6 show the adjusted probability of the various outcome definitions for outlets that “had an employee who received training on the AMFm QAACTs” (yes/no) in private and public sector outlets respectively. The adjusted probabilities of QAACT availability for the variable rural/urban and the other outlet and respondent characteristics that were statistically significant in the unadjusted analysis of weighted percentages of outlets with the outcomes (shown in Table 4), are also included in Tables 5 and 6.

Although in the adjusted analysis, training remained a significant predictor of the first two outcomes (availability of QAACTs and co-paid QAACTs) in private sector outlets ($p=0.039$ and $p=0.020$), it was not a predictor of any of the outcomes in the public sector. On the other hand, “Category of highest health-related qualification or training of at least 1 staff” was a highly significant predictor of all definitions of QAACT availability among both private and public outlets. For all outcome definitions, the predicted probability of QAACT availability in private sector outlets increased from

those that had at least 1 staff with no health-related qualification, to those that had qualifications other than for prescribing or dispensing, to those that had formally trained prescribers/dispensers. However the trend in association between health-related qualification and our outcomes was the opposite in public sector outlets, although all outlets had at least one employee with a health-related qualification.

After adjusting for other covariates, the number of prescribers/dispensers in an outlet remained a significant predictor of QAACT availability in public sector outlets irrespective of how it was defined. Outlets with higher numbers of prescribers had a higher predicted probability of the outcomes. On the other hand, among private sector outlets, though the trend in association was the same as in the public sector, the number of prescribers/dispensers was a significant predictor only of stocking “at least 1 co-paid QAACT without stocking any AMTs or nATs” ($p=0.001$).

Both the public and private sector show interesting variation by effect and trend with respect to malaria epidemiologic zone after adjusting for covariates in the separate models. In the private sector for instance, although not statistically significant, there was a positive correlation between malaria epidemiologic zone and the outcomes: “stocked QAACTs” and “stocked co-paid QAACTs” i.e. predicted probability of the two outcomes increased from the northern zone through to the coastal zone. However the direction of this correlation was reversed for our most conservative outcome measure; stocked “at least 1 co-paid QAACT without stocking any AMTs or nATs”, and this was statistically significant ($p=0.011$). In the public sector however, malaria epidemiologic zone remained a significant predictor of all definitions of QAACT availability. The pattern of predicted probability being highest in the northern savanna zone, followed by the coastal zone and

then the forest zone having the relatively lowest predicted probability, was consistent across all the outcome definitions in the public sector.

Discussion

The AMFm Phase 1 pilot involved a factory-gate subsidy on “green leaf logo” branded, quality-assured ACTs (QAACTs), and one of the objectives of the intervention was to “increase ACT availability” (The Global Fund, 2009b). Therefore in this study, we declared the outcome of interest broadly as the availability of quality-assured ACTs (QAACTs) in an outlet, and further examined this outcome with specific reference to availability of QAACTs with the AMFm “green leaf logo” (co-paid ACTs). However another objective of the AMFm intervention with respect to availability was to “crowd out” oral artemisinin monotherapies (AMTs) and non-artemisinin therapies (nATs). Thus we further scrutinized the intervention by investigating to what degree outlets stocked at least 1 co-paid QAACT without stocking any AMTs or nATs.

Pre-existing differences in characteristics and the complex interconnectedness of the public and private antimalarial markets in Ghana, may explain why even carefully thought out and executed interventions like the AMFm yielded varying degrees of success across sectors. For example, as has been shown in many sub-Saharan countries (Albertini et al., 2012), including Ghana (Chandler, Whitty, & Ansah, 2010), malaria testing was barely available in the private sector (4.5% of outlets), while 40% of public sector outlets offered malaria testing. Also, while a high percentage of public (75.3%) and private (84.1%) outlets stocked at least 1 co-paid QAACT, a large difference between the two sectors emerged (71% vs. 20.1%) when not stocking AMTs and nATs

was included in the outcome definition. Thankfully, only 1.7% and 3% of public sector outlets stocked AMTs and nATs respectively, while deplorably, 53.7% and 52.9% of private sector outlets stocked the same. These findings indicate that despite high QAACT availability in the private sector, the desired policy goal of crowding out AMTs and nATs requires further attention.

We found that at the time of the interview and antimalarial audit, 80% and 87% of public and private sector outlets respectively stocked at least 1 QAACT. Furthermore, only 5.8% (14) of public, and 3.2% (18) of those private sector outlets that stocked at least 1 QAACT, did not stock any co-paid QAACTs. This is encouraging, and maintaining a reliable supply-chain while minimizing the shortage (stock-out) of ACTs in outlets is an important component of market-based malaria interventions such as the AMFm and a key ingredient for success (Cohen et al., 2010; Kindermans, Pilloy, Oliaro, & Gomes, 2007; Shretta & Yadav, 2012; Yadav et al., 2012). Only 1.65% of public and 1.78% of private sector QAACT stocking outlets had experienced shortages (stock-outs) for at least 1 day in the last 7 days leading up to the interview and antimalarial audit. These low stock-out levels are encouraging, contrary to the documented pattern of frequent stock-outs of ACTs, in both public and private sector outlets (J. H. Amuasi et al., 2012; B. B. Kangwana et al., 2009; Zurovac et al., 2008), and are a positive find suggestive of a stable antimalarial supply chain in Ghana.

While various supporting interventions within the framework of a large intervention such as the AMFm, have the potential to modify key provider/outlet and consumer characteristics to enhance desired outcomes, other characteristics cannot easily be modified. For example malaria epidemiologic zone, rural urban differences, and

variation in number of prescribers/dispensers have the potential to impact on the outcomes of complex interventions like the AMFm. Nevertheless, policy makers need an understanding of how both the modifiable and less-modifiable characteristics of providers/outlets and consumers, their geographies, and economies function, so as to inform the design and implementation of effective interventions such as the AMFm (Craig et al., 2008; de Savigny & Adam, 2009; Habicht et al., 1999). Understanding factors accounting for the outcomes of the AMFm in Ghana is additionally important, considering that the Ghana Ministry of Health has indicated its willing to commit some of its Global Fund resources to antimalarial drug subsidies after the AMFm.

For the implementation of malaria control interventions to be successful, it is critical that both providers and consumers are empowered with adequate knowledge, which can be achieved through training (B. P. Kangwana et al., 2013). In a recent systematic review, Wafula et al show that knowledge is able to induce compliance/action, whether it be using ACTs, adhering to treatment regimen, or purchasing and sleeping under bed nets (Wafula, Miriti, & Goodman, 2012). Key supporting interventions to the AMFm included training staff of both public and private sector outlets on the need to use QAACTs for treating uncomplicated malaria and on the green leaf logo as an identifier for the co-paid QAACTs (J. Amuasi et al., 2012; RBM Partnership, 2013; Tougher et al., 2012).

From our adjusted analysis in the private sector, training was a predictor of stocking QAACTs in general and specifically, co-paid QAACTs. Similar to our findings, a study conducted by the Clinton Health Access Initiative in Madagascar, another AMFm phase 1 pilot country, showed that in the private sector, training via academic detailing

was directly linked to an increase in ACT stocking (Ward, Lesage, Morris, Lam, & Cohen, 2012). The importance of training in the private sector is further emphasized by the positive correlation between training and even the very conservative outcome definition of stocking at least 1 co-paid QAACT without stocking any AMTs or nATs, although this was not statistically significant ($p=0.171$).

Our findings further suggest that while trainings such as workshops and seminars might be important for improving availability of recommended ACTs in private sector outlets, training alone might not suffice if removal of AMTs and nATs from their shelves is to be achieved. Research carried out among private sector outlets in Uganda (also an AMFm phase 1 pilot country) showed that although shop assistants were less likely to attend training sessions, those that attended did not necessarily have any higher probability of being able to correctly identify the recommended first-line treatment than those who did not attend (Rusk et al., 2012). Another Uganda-based study also showed that malaria in-service training did not significantly predict health worker selection of an ACT for treating uncomplicated malaria (Zurovac et al., 2008). Thus it is possible that since training focused on the AMFm QAACTs, it might be associated with stocking QAACTs, but might not necessarily be associated with a deep knowledge about malaria treatment, allowing outlets to persist in stocking the non-recommended AMTs and nATs.

The insignificance of training for predicting any of our outcomes in public sector outlets is however not surprising. This is because in the public sector, stocking decisions are made centrally (at district and regional level). Thus the presence or absence of training becomes less important for predicting stocking in the public sector. In the private sector however, stocking decisions are often made by the outlet owner or manager in

consultation with prescribers/dispensers and based on consumer demand, reflected by sales figures.

While basically high QAACT availability was achieved post the AMFm across both sectors, the centralized nature of public sector commodity procurement and service delivery mechanisms makes it simpler to achieve adherence to antimalarial policy with respect to not stocking AMTs and nATs. On the other hand private sector procurement is largely driven by demand and profit margins (Shretta & Yadav, 2012). Approaches to improving policy adherence in the private sector, such as imposing severe penalties on importers of oral AMTs and nATs, coupled with explicit campaigns vilifying their use for the treatment of uncomplicated malaria, are therefore worth considering by policy makers. As of now, most campaigns have focused on the positives of using QAACTs without stressing much on the negatives of using AMTs and nATs. Negative campaigning as a means of modifying demand and supply patterns has been shown to be successful in many spheres, including where health, public policy, and politics intersect (Beaudoin, Fernandez, Wall, & Farley, 2007; Dixon, Scully, Wakefield, White, & Crawford, 2007; Emery, Szczypka, Powell, & Chaloupka, 2007; Frieden, Dietz, & Collins, 2010; Hanenberg & Rojanapithayakorn, 1998; Hoffman, 2003; Kearney, 2010; Orleans, 2007; Wakefield, Loken, & Hornik, 9).

Almost 100% of staff in public sector outlets had a health-related qualification as against 67% of private sector outlets. The positive and statistically significant trend in the relationship between health-related qualifications and all definitions of QAACT availability in the private sector is consistent with the impact of training on our stocking outcomes. It is therefore reasonable to infer that in the private sector, the more

sophisticated the retailer (having received training on co-paid QAACTs and having a health-related qualification), the more likely they were to have positive stocking outcomes.

In the public sector however, although also statistically significant we found a negative trend in the relationship between health qualification and stocking outcomes. Although all public sector outlets by default have at least 1 employee with some health-related qualification, we found that those outlets with an employee formally trained to prescribe or dispense medications had lower predicted probabilities of the outcomes compared to outlets with only employees without formal training or certification for prescribing or dispensing medications. While this negative association is counter intuitive and requires further analyses to explain, it at least indicates how differently from each other the public and private sectors behave.

Although slightly different with respect to the outcome measure, private sector findings are echoed by other research. A recent study conducted among private sector outlets in Uganda showed that having a formal health-related qualification significantly predicted correctly identifying policy recommended antimalarials (Rusk et al., 2012). An older study also conducted in Uganda, showed that being a formally trained health worker significantly predicted selection of an ACT for treatment (Zurovac et al., 2008).

The importance of health-related qualification and training in the private sector is further reflected in the association between availability of malaria testing and the outcome: “stocked at least 1 co-paid QAACT without stocking any AMTs or nATs”. Based on this association, although further analyses are required, we hypothesize that an outlet with qualified and/or trained personnel is more likely to recognize the importance

of testing before treating malaria, and so will offer testing. By extension, staff in outlets where tests are available are also likely to know the recommended treatment to offer, and therefore would stock co-paid QAACTs and not AMTs or nATs.

Our study also showed that the number of dispensers/prescribers was significantly positively associated with all QAACT stocking measures in the public sector. Here, for all three stocking outcome definitions, outlets that had 3-4, and those that had 5 or more prescribers/dispensers, had the same predicted probabilities of the stocking outcomes, both of which were about 20% higher than that for outlets with 1-2 prescribers/dispensers. This lower probability of the outcomes in smaller public sector outlets could reflect the increased opportunity for non-adherence to policy and for malfeasance among outlets with just 1 or two staff, coupled with lower levels of central supervision, given that these are often found in more rural and hard-to-reach areas. In the private sector however, number of dispensers/prescribers was significantly associated only with stocking “at least 1 co-paid QAACT without stocking any AMTs or nATs”. Nevertheless we found a generally positive correlation between increasing number of dispensers/prescribers and the probability of the stocking outcomes. In a related study following the AMFm in Kenya, O’Meara et al also showed that a higher number of prescribers in an outlet was associated with more desirable stocking practices (O’Meara et al., 2013). Our findings suggest that efforts at improving QAACT stocking need to pay special attention to smaller outlets with less than 5 prescribers/dispensers.

The coastal and forest zones include Accra (the capital) and Kumasi respectively, which are both bustling cities with high economic activity. Both zones also contain most of the economic wealth of the country, and their inhabitants generally have higher

socioeconomic status relative to the northern savanna zone. Malaria prevalence is generally highest in the northern savanna zone and lowest in the coastal zone (GSS, 2011). The co-paid QAACTs were much more affordable than other QAACTs, AMTs and most nATs (J. Amuasi et al., 2012). From the above, taking malaria prevalence and socio-economic status into consideration, in the private sector, the higher probability of stocking “at least 1 co-paid QAACT without stocking any AMTs or nATs” in the northern savanna zone relative to the coastal (lowest probability) and forest zones is understandable. It is also possible that in the coastal and forest zones where people are wealthier, the less expensive co-paid QAACTs were perceived to be less “powerful” than the well-known, more expensive non-subsidized QAACTs without the logo, AMTs or nATs. Therefore if consumers could afford the better known, more expensive antimalarials, they might have preferred to buy them over the much less expensive AMFm co-paid QAACTs. Prescribers and dispensers eager to exhaust their stock of relatively more expensive AMTs and nATs were perhaps also more likely to recommend and sell them to consumers whom they perceived as having greater purchasing power.

We had earlier asserted that adherence to antimalarial policy was more easily achieved in the public sector, owing to the centralized nature of public sector commodity procurement and service delivery mechanisms. The combination of central control stocking choice constraints, affordability of the co-paid QAACTs relative to AMTs and nATs, together with the generally lower purchasing power in the northern zone, may account for it having the highest predicted probability for all definitions of the QAACT stocking outcomes. However this hypothesis does not fit with our observation of the forest zone having a lower predicted probability of stocking QAACTs defined in any way

compared to the coastal zone, given that the coastal sector is arguably wealthier than the forest zone. It could be that a combination of various geographic, socio-economic, and public sector ease of policy implementation factors interact in more complicated ways to yield this picture, calling for further research.

There are a number of limitations to our study. We are constrained to explaining stocking of QAACTs primarily using variables available from the AMFm endline IE survey. There are additional factors that may explain QAACT stocking, such as variations in socio-economic standing of surveyed clusters, which we could not include in our models. In Ghana epidemiologic zones with higher malaria prevalence levels are often found in areas of low socio-economic status (Gardiner, Biggar, Collins, & Nkrumah, 1984). Nevertheless factors such as local population density, fever prevalence and measures of wealth have been suggested to have no correlation with ACT stocking and sales practices (O'Meara et al., 2013).

Another limitation of concern is that some of the data obtained with respect to outlet characteristics was reported by respondents and was not directly observed, increasing the risk of reporting bias. Of particular concern are the data on training and qualifications, where over-reporting has been recognized in similar studies as a challenge (Rusk et al., 2012). It is also important to bear in mind that determinants of stocking practices may differ from determinants of prescribing/dispensing practice, and from determinants of use patterns. Antimalarial use patterns are what directly impacts on malaria morbidity and mortality.

Our research findings confirm that while the private and public antimalarial markets are interconnected and complimentary in nature, the private sector market is

much larger and less aligned with national policy. The complicated nature of the private sector makes it difficult to regulate and monitor. We also find that predictors of antimalarial stocking vary considerably between the two sectors. These variations call for different approaches or emphasis to be placed on various aspects of interventions like the AMFm in the public and private sectors.

While especially in the private sector, “in-service” training was generally shown to be an important tool towards improving ACT stocking practices and should continue to be promoted. Getting outlets to hire staff with health-related qualifications should also be pursued as an effective longer-term approach towards achieving ACT stocking benchmarks and recommended treatment practice. Also, in carrying out training, extra effort must be made to ensure that smaller outlets (especially those with 1-2 employees) are specially targeted and covered.

This work is an important addition to the gradually expanding body of knowledge being gathered from the AMFm experience in the various pilot countries and, is of importance as several countries consider the best use of their Global Fund malaria allocations, including towards subsidies on ACTs in both their public and private sectors.

Table 2: Independent variables

Independent variables	Categories
<i>Main predictor variable</i>	
An employee from the outlet received training on QAACts with the logo	Yes/No
<i>Other variables</i>	
Malaria testing (microscopy/RDT) available	Yes/No
Respondent owned the outlet	Yes/No
At least 1 employee had completed secondary/high school	Yes/No
Location	Rural/Urban
Malaria epidemiologic zone*	Coastal/ Forest/ Savanna
Highest health-related qualification of at least one employee	None/ Not trained or certified to prescribe or dispense [‡] / Trained or certified to prescribe or dispense [°]
Number of prescribers/dispensers employed	1-2/ 3-4/ 5 or more
<p><i>*Approximation based on demarcations of ecological zones (Coastal, Forest and Savanna) used by the Ghana Statistical Service</i></p> <p><i>[‡]Examples include: laboratory technician, healthcare assistant etc.</i></p> <p><i>[°]Comprises any of the following: Nurse/midwife, pharmacist/dispensing technician, medical doctor/medical assistant</i></p>	

Table 3: Unweighted distribution of outlet characteristics

Characteristics		*Type of outlet, n or N (%)		
		Public n = 303 (31.9)	Private n = 648 (68.1)	All N = 951 (100)
Stocked an antimalarial		298 (98.4)	642 (99.1)	940 (98.8)
Stocked at least 1 QAACTs		242 (79.9)	563 (86.9)	805 (84.7)
Stocked at least 1 co-paid QAACTs		228 (75.3)	545 (84.1)	773 (81.3)
Stocked at least 1 SP or Quinine		175 (57.8)	436 (67.3)	611 (64.3)
Stocked at least 1 oral AMT		5 (1.7)	348 (53.7)	353 (37.1)
Stocked at least 1 nATs**		9 (3)	343 (52.9)	352 (37)
Stocked at least 1 antimalarial used for prophylaxis or no longer used for treatment		0	19 (2.9)	19 (2)
Stocked at least 1 co-paid QAACTs without stocking any AMTs or nATs**		215 (71)	130 (20.1)	345 (36.2)
An employee from the outlet received training on QAACTs with the logo		178 (58.8)	298 (46)	476 (50.1)
Malaria testing (microscopy/RDT) available		121 (39.9)	29 (4.5)	150 (15.8)
Respondent owned the outlet		N/A	237 (36.6)	237 (24.9)
At least 1 employee had completed secondary/high school		293 (96.7)	598 (92.3)	891 (93.7)
Location	Urban	95 (31.4)	474 (73.2)	569 (59.8)
	Rural	208 (68.7)	174 (26.9)	381 (40.2)
Malaria epidemiologic zone [§]	Coastal savanna/Mangrove swamps	73 (24.1)	310 (47.9)	383 (40.3)
	Tropical rain forest	151 (49.8)	247 (38.1)	398 (41.9)
	Northern savanna	79 (26.1)	91 (14)	170 (17.9)
Category of highest health-related qualification	Non-health-related	2 (0.7)	181 (27.9)	183 (19.2)
	[¶] No formal training or certification for prescribing or dispensing medications	27 (8.9)	102 (15.7)	129 (13.6)
	[°] Formally trained to prescribe or dispense medications	256 (84.5)	333 (51.4)	589 (61.9)
Number of prescribers/dispensers employed	1 - 2	141 (46.5)	381 (58.8)	522 (54.9)
	3 - 4	103 (34)	210 (32.4)	313 (32.9)
	5 or more	57 (18.8)	53 (8.2)	110 (11.6)
Survey weighted mean number of prescribers/dispensers employed (95% CI)		3.6 (3.1, 4)	2.2 (2.1, 2.4)	2.4 (2.2, 2.5)
Survey weighted mean number of antimalarials audited (95% CI)		4 (3.6, 4.4)	7.3 (6.6, 7.9)	6.9 (6.2, 7.5)

*Percentages may not total 100 because of rounding or missing data

**Excludes SP, Quinine, and those antimalarials used strictly for prophylaxis or no longer for treatment

[¶]Examples include: laboratory technician, healthcare assistant etc.

[°]Comprises any of the following: Nurse/midwife, pharmacist/dispensing technician, medical doctor/medical assistant

[§]Approximation based on demarcations of ecological zones (Coastal, Forest and Savanna) used by the Ghana Statistical Service

Table 4: Survey weighted percentage of outlets with the outcomes

Variables		Stocked some QAACTs				Stocked some co-paid QAACTs				Stocked some co-paid QAACTs without stocking any AMTs or nATs			
		Private, N = 563		Public, N = 242		Private, N = 545		Public, N = 228		Private, N = 130		Public, N = 215	
		w%	p-value	w%	p-value	w%	p-value	w%	p-value	w%	p-value	w%	p-value
At least 1 employee from the outlet had received training on QAACTs with the logo	Yes	86.1	*0.032	77.8	0.824	84.8	*0.020	73.6	0.989	23	0.144	69.9	0.961
	No	75.3		79.1		73		73.6		18.1		70.2	
Malaria testing (microscopy/RDT) available	Yes	88.4	0.352	77.9	0.565	88.5	0.256	70.2	0.303	54.5	*0.000	66.1	0.287
	No	81.3		80.9		79.3		77.8		18.6		73.9	
Respondent owned the outlet	Yes	78.9	0.190	-	-	77.6	0.369	-	-	19.7	0.696	-	-
	No	83.2		-		80.8		-		20.9		-	
At least 1 employee had completed secondary school	Yes	83.4	*0.000	-	-	81.7	*0.000	-	-	20.1	0.731	-	-
	No	62.2		-		59.8		-		22		-	
Category of highest health-related qualification	Non-health-related	72.9		-		71.2		-		14.3		-	
	[¶] No formal training or certification for prescribing or dispensing medications	80.4	*0.000	91.7	0.070	78.8	*0.000	85.6	0.116	21.5	*0.002	85.6	*0.047
	[°] Formally trained to prescribe or dispense medications	94.7		78.9		92.7		74.7		28.4		71.5	
Number of prescribers/dispensers employed	1 - 2	79.2		71.5		77.5		65.6		19		63.9	
	3 - 4	86.2	\$0.040	84.4	*0.007	83.5	*0.004	80.8	*0.007	19.1	*0.000	75.5	0.075
	5 or more	\$-		89		97.2		83.3		44.7		76.9	

P-values were derived from χ^2 tests of significance for differences in the survey weighted distribution of each variable for the outcomes, between its categories. "Yes", "Non-health-related", "1 - 2", "Rural", and "Coastal savanna" were reference groups. This is analogous to "univariate" logistic regressions

**Statistically significant p-value (≤ 0.05)*

[¶]Examples include: laboratory technician, healthcare assistant etc.

[°]Comprises any of the following: Nurse/midwife, pharmacist/dispensing technician, medical doctor/medical assistant

^{\$}All 53 private sector outlets with more than 5 prescribers stocked at least 1 QAACT and so were excluded by STATA from the analysis

***Approximation based on demarcations of ecological zones (Coastal, Forest and Savanna) used by the Ghana Statistical Service*

Table 4 (Continued): Survey weighted percentage of outlets with the outcomes

Variables		Stocked some QAACTs				Stocked some co-paid QAACTs				Stocked some co-paid QAACTs without stocking any AMTs or nATs			
		Private, N = 563		Public, N = 242		Private, N = 545		Public, N = 228		Private, N = 130		Public, N = 215	
		w%	p-value	w%	P-value	w%	p-value	w%	P-value	w%	p-value	w%	P-value
Location	Rural	74.1	*0.026	82.6	0.181	71.4	*0.015	76.2	0.536	17.5	0.237	73.9	0.269
	Urban	85.4		72.3		83.9		70.6		21.9		63	
Malaria epidemiologic zone**	Coastal savanna	86.5		79.4		84.6		73.1		16.6		66	
	Tropical rain forest	82.5	*0.024	73	*0.032	80.4	*0.029	67.4	*0.031	22.8	0.153	62.8	*0.007
	Northern savanna	67.2		91.6		65.7		89		22.5		89	

P-values were derived from χ^2 tests of significance for differences in the survey weighted distribution of each variable for the outcomes, between its categories. "Yes", "Non-health-related", "1-2", "Rural", and "Coastal savanna" were reference groups. This is analogous to "univariate" logistic regressions

*Statistically significant p-value (≤ 0.05)

°Examples include: laboratory technician, healthcare assistant etc.

°Comprises any of the following: Nurse/midwife, pharmacist/dispensing technician, medical doctor/medical assistant

§All 53 private sector outlets with more than 5 prescribers stocked at least 1 QAACT and so were excluded by STATA from the analysis

**Approximation based on demarcations of ecological zones (Coastal, Forest and Savanna) used by the Ghana Statistical Service

Table 5: Adjusted probability of outcomes in PRIVATE sector outlets

Variables		Stocked at least 1 QAACT		Stocked at least 1 co-paid QAACT		Stocked at least 1 co-paid QAACT without stocking any AMTs or nATs	
		N = 563		N = 545		N = 130	
		Pr	p-value	Pr	p-value	Pr	p-value
At least 1 employee from the outlet received training on QAACTs with the logo	Yes	85.2		84.9		22.9	
	No	76.6	*0.039	75.8	*0.020	18	0.171
Malaria testing (microscopy/RDT) available	Yes	74.4		78.3		48.4	
	No	81.3	0.445	80.8	0.767	19.2	*0.000
At least 1 employee had completed secondary school	Yes	81.6		81.3		19.7	
	No	78.5	0.513	76.8	0.371	33.6	0.056
Non-health-related		75		74.6		13.8	
Category of highest health-related qualification	[‡] No formal training or certification for prescribing or dispensing medications	78.5	*0.000	78.6	*0.000	25.3	*0.006
	[°] Formally trained to prescribe or dispense medications	92.9		91.1		27.4	
Number of prescribers/dispensers employed	1 - 2	80.6		80.3		20.9	
	3 - 4	83.8	§0.450	81.2	0.217	16.5	*0.001
	5 or more	§		92.3		35.6	
Location	Rural	80.1	0.620	79	0.465	17.1	0.136
	Urban	82		81.9		22.6	
Malaria epidemiologic zone**	Coastal savanna	83.6		82.1		16	
	Tropical rain forest	81.7	0.348	81.8	0.344	22.2	*0.011
	Northern savanna	76.1		75.8		30.5	

P-values were derived from χ^2 tests of significance of the differences in adjusted survey weighted predicted probabilities of the outcomes for the categories of each variable. "Yes", "Non-health-related", "1-2", "Rural", and "Coastal savanna" were reference groups

*Statistically significant p-value (≤ 0.05)

[‡]Examples include: laboratory technician, healthcare assistant etc.

[°]Comprises any of the following: Nurse/midwife, pharmacist/dispensing technician, medical doctor/medical assistant

[§]All 53 private sector outlets with more than 5 prescribers stocked at least 1 QAACT and so were excluded by STATA from the analysis

Table 6: Adjusted probability of outcomes in PUBLIC sector outlets

Variables		Stocked at least 1 QAACT		Stocked at least 1 co-paid QAACT		Stocked at least 1 co- paid QAACT without stocking any AMTs or nATs	
		N = 242		N = 228		N = 215	
		Pr	p-value	Pr	p-value	Pr	p-value
At least 1 employee from the outlet received training on QAACTs with the logo	Yes	79.1	0.974	74.1	0.823	71.5	0.905
	No	79.2		75.7		72.4	
Category of highest health-related qualification	Non-health-related ‡No formal training or certification for prescribing or dispensing medications	N/A		N/A		N/A	
	°Formally trained to prescribe or dispense medications	93.6	*0.006	90.4	*0.007	90.5	*0.002
		77.2		72.9		69.7	
Number of prescribers/dispensers employed	1 - 2	69.4		64.7		62.6	
	3 - 4	87.2	*0.001	83.2	*0.005	79.9	*0.007
	5 or more	87.3		83.1		79.2	
Location	Rural	81.5	0.294	74.8	0.978	72.6	0.794
	Urban	73.7		74.5		70.3	
Malaria epidemiologic zone**	Coastal savanna	79.4		71.8		68.2	
	Tropical rain forest	72.6	*0.029	67.3	*0.026	63.4	*0.009
	Northern savanna	90.7		89.6		89.4	
P-values were derived from χ2 tests of significance of the differences in adjusted weighted predicted probabilities of the outcomes for the categories of each variable. "Yes", "Non-health-related", "1 - 2", "Rural", and "Coastal savanna" were reference groups							
*Statistically significant p-value (≤0.05)							
‡Examples include: laboratory technician, healthcare assistant etc.							
°Comprises any of the following: Nurse/midwife, pharmacist/dispensing technician, medical doctor/medical assistant							

Chapter 4: The AMFm in Ghana: Factors Associated with Private Retailer's

Adherence to the Recommended Retail Price

Introduction

The Affordable Medicines Facility-malaria (AMFm) was initiated as a pilot in 7 countries aimed at increasing availability, reducing prices, increasing market share and increasing use of co-paid quality-assured artemisinin-based combination therapies (QAACTs). As part of the AMFm supporting interventions to facilitate the high level subsidy on QAACTs reaching consumers, the AMFm green leaf-logo was widely publicized, along with a recommended retail price (RRP) in Ghana.

Using data from the 2011 endline survey of the Global Fund-commissioned AMFm independent evaluation, we explored factors associated with outlets stocking some co-paid QAACTs at RRP, and those stocking all at RRP in the private-for-profit health sector in Ghana. Analyses accounted for the complex survey design. We used multivariate logistic regressions to determine the association between being aware of the RRP and correctly specifying it, and the probability of stocking some or all QAACTs at RRP.

Among the 545 outlets making up our sample, and which stocked at least 1 co-paid QAACT, 1,440 co-paid QAACTs were audited, with a mean number of 2.3 per outlet (95% CI: 2.1, 2.4). Twenty-four percent of outlets stocked no co-paid QAACTs at RRP, while 68% had some, but not all their co-paid QAACTs at RRP. Almost half of all the co-paid QAACTs audited were available at RRP. Many more outlets stocked some

co-paid AL compared to those that stocked some ASAQ (93 % vs. 46%). Knowledge of the RRP was associated with a much higher predicted probability of stocking some co-paid QAACTs at RRP than stocking all at RRP (83% vs. 41%), although it was a strong predictor of both outcomes ($p < 0.001$ for both). The type of co-paid QAACT being stocked (ASAQ, AL, or both) was an important predictor of an outlet stocking both some ($p = 0.014$) and all ($p = 0.005$) co-paid QAACTs at RRP. Malaria prevalence was also associated with stocking some co-paid QAACTs at RRP ($p = 0.013$).

Our study shows that retailer's adherence to the RRP for co-paid QAACTs can be high when knowledge about the RRP is present. Information on the AMFm subsidy needs to be disseminated to retailers with greater focus on those areas of high malaria prevalence, such as the northern savanna zone. All recommended policy interventions should be coupled with regular monitoring of prices and other indicators in the market in order to accurately measure the trend of the effects of the interventions.

Background

In Ghana, health facility data shows that malaria accounts for 38.2% of all outpatient illnesses, 34.9% of all admissions, and 34% of all deaths in children under 5 years in Ghana (NMCP, 2010). At the country level, high mortality from malaria is strongly correlated with lower gross national income per capita, while at the individual level, mortality is strongly associated with living on less than USD 1.25 per person per day (Worrall, Basu, & Hanson, 2005). Economic inequality, leading to competition for resources, is a major cause of persistent disparities in health outcomes along socio-economic lines (Wilkinson, 1997; Willson, 2009), despite significant improvements in overall population health (Link, 2008; Marmot, 2002). Therefore the poor become not only more susceptible to getting malaria, but are also less able to access and afford effective treatment (Arrow et al., 2004; Worrall et al., 2005).

Since 2001, the World Health Organization (WHO) has recommended artemisinin-based combination therapies (ACTs) as first-line treatment for uncomplicated *P. falciparum* malaria (WHO, 2006). However, ACTs have remained relatively expensive to manufacture. High quality ACTs averaged around USD 10.00 per adult treatment, making them unaffordable to many patients in malaria endemic countries, whose disposable income ranges from USD1 to USD 2 per day (RBM Partnership, 2013). The limited availability and relatively high prices of high quality ACTs particularly in rural areas, encourages treatment with other, more common, and usually much less expensive, antimalarials, though these are less effective and often of poor quality. Thus the uptake of high quality ACTs has been slow (O. J. Sabot et al., 2009).

To address the problem of cost as a barrier to access, the public health sectors of many malaria endemic countries have introduced a policy of free or highly subsidized distribution of ACTs to patients. Despite these efforts, the limited number and access offered by the public sector, coupled with the high cost of quality ACTs in the private sector, led major global malaria stakeholders to adopt the Affordable Medicines Facility – malaria (AMFm) in 2010 (Cohen et al., 2010; Goodman et al., 2009; Littrell et al., 2011; The Global Fund, 2012a). The AMFm was based on evidence that increasing the availability of ACTs and lowering the price paid by the end user could be an effective way to increase their uptake (Arrow et al., 2004; R. Laxminarayan et al., 2006; Moszynski, 2008) and crowd out non-ACTs by gaining market share (The Global Fund, 2009b).

The AMFm involved a factory-gate co-payment of up to 95% of the cost of quality assured ACTs (QAACTs) on behalf of public and private sector first-line buyers (FLBs), along with a number of supporting interventions. As part of the AMFm design, the ex-factory cost had already been drastically reduced following complex negotiations between the Global Fund to Fight Aids Tuberculosis and Malaria (The Global Fund – hosts of the AMFm secretariat) and manufacturers. The FLBs were required to pass on the massive cost savings to distributors (wholesalers and retailers) who were in-turn expected to finally pass them on to patients, so that the QAACTs would be affordable and therefore become the antimalarial of choice for even the most rural and poor populations (Dalberg Global Development Advisors, 2007). Although the final price to consumers was not formally restricted in the AMFm design, the Ghana AMFm Coordinating

Committee in consultation with the private sector, determined and widely publicized a recommended retail price (RRP) for the QAACTs of USD 0.96 per treatment (J. Amuasi et al., 2012). The co-paid QAACTs were made easily identifiable by a logo depicting a green leaf on their packaging, which we refer to as the “AMFm Logo”.

The AMFm was a 2-year pilot intervention in seven countries including Ghana. By measuring changes between baseline and endline surveys in availability, price, market share and use of QAACTs, a Global Fund commissioned Independent Evaluation (IE) of the impact of the AMFm phase I was carried out in each pilot country (AMFm IE Team, 2012; The Global Fund, 2009a). Among private sector outlets in Ghana, the median endline price of co-paid QAACTs was the same as the RRP of USD 0.96 (2010 prices), whereas QAACTs without the AMFm logo had a very high median price of USD 7.51 (J. Amuasi et al., 2012; J. Amuasi, Nguah, Diap, Buabeng, & The Independent Evaluation Team, 2011).

Although subsidies have been shown to lower the prices of antimalarial drugs significantly (N. Smith et al., 2011), during monitoring of the AMFm Phase I in Ghana, there were reports suggesting that some retailers were capturing the AMFm subsidy by not adhering to the RRP and were selling the co-paid ACTs at more than 200% of the approved price, making super-normal profits (Cofie, 2011; Daily Graphic, 2011). Monitoring reports from other countries also suggested that retailers took advantage of the subsidy to maximize profits with wide variations in pricing of the co-paid ACTs between USD 0.25 and USD 3.00. Some retailers claimed that they had to inflate the prices beyond the RRP simply because if they adhered to it, they would make overall

losses when costs of transporting the drugs and other inputs were taken into consideration. Some retailers did not stock the co-paid ACTs at all because they claimed the profit margins from them were simply too small and sales volumes were not high enough (Esipisu, 2011).

At the end of the AMFm phase I, the Roll Back Malaria (RBM) Partnership hosted by the World Health Organization (WHO), described the AMFm as having a “*dramatic impact on the antimalarial market*” in the private sector; including large decreases in ACT prices (RBM Partnership, 2013) [page 8]. More recently, results from a systematic review of available indicate that the AMFm subsidy led to an increase in the use of private sector QAACs (Morris, Ward, Moonen, Sabot, & Cohen, 2014). In this paper we explore outlet characteristics that were associated with private for-profit sector outlets stocking co-paid QAACs at or below the recommended retail price (RRP) of USD 0.96.

Methods

Data Source

The AMFm Independent Evaluation endline survey was carried out in late 2011 and was our main source of data. The survey was based on a non-experimental design with assessment of key indicators in rural and urban domains on a national scale. The data collection, analysis process and findings of the IE are described in other sources (J. Amuasi et al., 2012; Tougher et al., 2012; Willey et al., 2014). Shapefiles and other geographic information systems data on districts in Ghana were obtained from the Centre

for Remote Sensing and Geographic Information Services of the University of Ghana via ESRI's GeoCommons platform (CERSGIS, 2012). Data on *Plasmodium falciparum* malaria prevalence by district were obtained from the 2010 posterior predictive distribution model estimates produced by the Malaria Atlas Project (MAP). Further details on the MAP methodology are available from other publications (Gething et al., 2011; MAP, 2010). Ethical clearance for the IE surveys in Ghana was obtained from the Ghana Health Service Ethical Review Committee on Research Involving Human Subjects (ERCRIHS). Our study was deemed not to fall within the University of Minnesota Institutional Review Board's regulatory definition of research with human subjects.

Data Management

A total of 765 private sector outlets contributed to the IE endline survey data. Our study sample included only outlets that were enumerated, completed the interview, and stocked some co-paid QAACTs. A total of 117 outlets fell into at least one of the following categories and so were excluded from the sample: 1.) Were not screened, 2.) Did not meet the screening criteria, 3.) Were not interviewed, 4.) Did not fully complete the interview and antimalarial audit, 5.) Were private not-for-profit facilities, and 6.) Did not have antimalarials in stock. A further 103 outlets did not stock any co-paid QAACTs and were also excluded from the sample.

The IE endline survey divided antimalarials into artemisinin-based combination therapies (ACTs) and non-ACTs. ACTs were subdivided into quality-assured ACTs (QAACTs) and normal ACTs (non-QAACTs). QAACTs were further classified into co-paid (had the AMFm logo) and non-co-paid. Details on the definition of QAACTs can be

found in other sources (AMFm IE Team, 2012). The non-ACTs were subdivided into three broad categories; non-artemisinin therapies (nATs), artemisinin monotherapies (AMTs), and antimalarials no longer used for treatment but only for prophylaxis (nRx). AMTs were further classified into oral and non-oral AMTs, while nATs were classified into Sulphadoxine-pyrimethamine (SP), which is recommended by the WHO for prophylaxis in pregnancy, quinine (for treating severe malaria), and other nATs. The endline survey data on outlet location was layered on the map of Ghana districts using ArcMap v10.2 (ESRI, 2013). The data on *Plasmodium falciparum* malaria prevalence by district was extracted from the MAP database and merged with the endline survey data using the “spatial join” feature in ArcMap.

Variables

Antimalarial prices and sales volumes are reported in terms of adult equivalent treatment doses (AETDs), determined using an AETD calculator, and is defined as the number of milligrams of an antimalarial drug needed to treat a 60 kg adult (Shewchuk et al., 2011). We investigated two distinct outlet-level outcomes: 1) Whether the outlet stocked at least one co-paid QAACT at or below the recommended retail price (RRP) (yes/no), and 2) whether all co-paid QAACTs stocked in an outlet were at or below the RRP (yes/no). We subsequently simplify the phrase “at or below the RRP” to “at RRP”. Whether or not the survey respondent knew there was a RRP for the QAACTs with the logo and was able to correctly specify it to be USD 0.96 was our main predictor investigated for both pricing outcomes.

A number of other factors and outlet characteristics potentially associated with QAACT pricing were included in the analysis, either directly or using proxies, such as *Falciparum* malaria prevalence (Pfpr), ownership, rural/urban status, stocking practices for QAACTs and other antimalarials, level of sophistication, size of the outlet, and malaria epidemiologic zone. Variables reflecting outlet sophistication included: availability of malaria testing; the survey respondent having completed secondary school; and having a pharmacist, nurse or doctor on staff. Variables describing outlet's stocking practices included whether the outlet stocked the antimalarials artesunate-amodiaquine (ASAQ), artemether-lumefantrine (AL) or both active ingredient types of QAACTs with the logo; adult, pediatric or both formulations of QAACTs with the logo; QAACTs without the logo; non-QAACTs; AMTs; or nATs.

We used the number of workers employed in the outlet and the number of different co-paid QAACTs stocked as proxies for outlet size. Both variables were included in our analysis after confirming that they do not pose the problem of multicollinearity. We recognize that it would be methodologically elegant to create a composite measure of size using number of workers and number of co-paid QAACTs stocked. However the two variables allow for an appreciation of the structure and nature of the outlets from different but equally important perspectives of size. Further discussion on the choice of proxies for outlet size can be found in Appendix 10.

Statistical Approach

For all analyses, we used the IE endline survey weights to account for the complex survey design used. We used t-tests to investigate how malaria prevalence

differed between rural and urban outlets and also among the three malaria epidemiologic zones: Coastal savanna/mangrove swamps, tropical rain forest, and northern savanna (see Table 3). The independent association between the outcome variables and continuous predictors (e.g. Pfpr, sales volume etc.), was also determined using t-tests of the difference in means of the predictors among outlets that had the pricing outcome vs. those that did not (see Table 2). We used chi-square tests to assess the unadjusted relationship between predictors that were expressed as binary or categorical variables and the pricing outcomes and (see Tables 4a and 4b).

We used multivariate logistic regressions to determine the association between malaria prevalence, knowing the AMFm and correctly specifying the RRP (knowledge), and the probability of our pricing outcomes. We adjusted/controlled for other variables that were statistically significant from our examination of the unadjusted relationships between independent variables and the pricing outcomes. Certain variables were excluded from the multivariate regression model due to concerns that they were highly correlated with other variables in the model. In all analyses, we performed several sensitivity analyses using alternate models, including using different variable categorizations, to confirm that the observed effects were not artifacts (see Appendices 11-14). P -values ≤ 0.05 were considered significant. All analyses were carried out using STATA v12 (StataCorp, 2012).

Results

Outlet Characteristics

There were 545 private-for-profit enumerated outlets which completed the interview and stocked at least 1 co-paid QAACT. Out of these, 412 stocked some (at least 1) co-paid QAACTs at or below the recommended retail price (RRP) of USD 0.96, and 173 outlets stocked all at RRP. Table 7 shows the distribution of the characteristics of outlets included in our study.

In 87% of outlets, the interviewee was aware there was a RRP and was able to correctly specify it as being USD 0.96 (knowledge). Knowledge was associated with a much higher predicted probability of stocking some co-paid QAACTs at RRP than stocking all co-paid QAACTs stocked at RRP (83% vs. 41%). Nevertheless in the unadjusted analyses, knowledge was a strong predictor of both stocking some QAACTs at RRP ($p<0.001$) and stocking all at RRP ($p=0.008$) (see Table 10a). Knowledge remained a strong predictor of both outcomes ($p<0.001$ for both) even after adjusting for other factors (see Tables 11 and 12).

Only 5% of outlets offered malaria tests to clients, and 35% of respondents owned the outlet (see Table 7). Although ownership status was associated with stocking all co-paid QAACTs at RRP ($p=0.002$) in the unadjusted analyses (see table 10a), this association disappeared after other factors were controlled for as shown in Table 12 ($p=0.217$). Without adjusting for other factors, an outlet having at least one employee being a pharmacist, nurse or doctor; and the number of employees, were strongly associated with the outlet stocking all co-paid QAACTs at RRP ($p=0.009$ and $p<0.001$

respectively). However after adjusting for other factors, both these associations were eliminated ($p=0.302$ and $p=0.272$ respectively) (see Tables 10a & 12). The mean number of employees per outlet in our sample was 2.5 (95% CI: 2.3, 2.7).

Stocking and sales volume

A total of 1,440 co-paid QAACTs were audited among the 545 outlets in our sample with a mean number of 2.3 QAACTs per outlet (95% CI: 2.1, 2.4) and a mean sales volume of 31.7 adult equivalent treatment doses (AETDs) per outlet (95% CI: 25.1, 38.3) over the week preceding the survey. The mean relative sales volume of co-paid QAACTs to all other antimalarials per outlet was 56.8% (95% CI: 53.2, 60.4). Out of the 1,440 QAACTs audited, 46.6% were stocked at RRP.

Ideally, an outlet should stock both adult and pediatric co-paid QAACTs at the RRP, however 24% of outlets in our sample stocked no co-paid QAACTs at RRP, while 68% had some, but not all their co-paid QAACTs at RRP. Only 27% of outlets had non co-paid QAACTs in stock and 81% had ACTs that were not QAACTs in stock. Many more outlets stocked some co-paid AL over ASAQ (93 % vs. 46%), and 54% stocked only co-paid AL while barely 7% stocked ASAQ only (see Table 7). Even after adjusting for other factors, the type of co-paid QAACTs being stocked (ASAQ/AL/both) was an important predictor of an outlet stocking both some ($p=0.014$) and all ($p=0.005$) co-paid QAACTs at RRP (see Tables 11 and 12, and Appendix 15). After adjusting for other factors, the predicted probability of all co-paid QAACTs in an outlet being sold at RRP was 46.8% for outlets that stocked adult co-paid QAACTs only and 8.7% for those that

stocked both adult and pediatric QAACTs ($p<0.001$) (see table 12). None of the 13 outlets that stocked only pediatric co-paid QAACTs had them at RRP (see Table 7).

At a mean number of 2.4 (95% CI: 2.2, 2.6) and 1.3 (95% CI: 1.2, 1.4) co-paid QAACTs per outlet for those that sold some and those that sold all co-paid QAACTs at RRP respectively, the number of co-paid QAACTs audited in an outlet was an important predictor of both pricing outcomes. After adjusting for other important factors, the number of co-paid QAACTs audited in an outlet was positively associated with the predicted probability of stocking some co-paid QAACTs at RRP ($p=0.082$). However, number of co-paid QAACTs in an outlet was negatively associated with the predicted probability of stocking all co-paid QAACTs at RRP ($p=<0.001$) (see Tables 11 & 12). The relationship between the number of co-paid QAACTs in an outlet and the proportion which are stocked at RRP is shown in Table 13 (also see Appendix 16).

Malaria prevalence and epidemiologic zones

From our sample, the mean prevalence of *falciparum* malaria (Pfpr) was 32.8% (95% CI: 28.3, 37.2) and ranged from 12.5 to 68.2%. Without adjusting for other factors, Pfpr was not associated with stocking some co-paid QAACTs at RRP ($p=0.722$). However after adjusting for other factors, a positive association became evident ($p=0.013$) with a 78% predicted probability of stocking some co-paid QAACTs at RRP among outlets within the highest Pfpr category (see Tables 10a & 11). On the other hand, without adjusting for other factors, Pfpr was positively associated with stocking all co-paid QAACTs at RRP ($p=0.008$), but the association was weakened after adjusting for other factors ($p=0.238$). This association between Pfpr and stocking all co-paid QAACTs

at RRP however remained positive, with a 40% predicted probability of stocking all co-paid QAACTs at RRP among outlets within the highest Pfpr category (see Tables 10a & 12, and Appendix 17).

Among both outlets that stocked some and those that stocked all co-paid QAACTs at RRP, the mean malaria prevalence was higher among outlets in rural compared to urban areas (39% vs. 30%, $p=0.014$ and 41% vs. 32%, $p=0.038$) respectively. Mean Pfpr also increased progressing from the coastal savanna to the northern savanna for both outlets that stocked some and all co-paid QAACTs at RRP ($p=0.001$ and $p<0.001$) respectively (see Table 9).

Discussion

The AMFm subsidy was applied directly by the Global Fund at the ex-factory level (top of the supply chain), and several factors act to influence markups applied throughout the chain by different actors (Palafox et al., 2014). Stakeholders were particularly concerned that retailers, who are the final interface between the patient and the QAACT, would seize the opportunity to make super-normal profits and not pass the subsidy on to consumers (O. Sabot et al., 2011). An outlet that stocked co-paid QAACTs, but sold them above and beyond the RRP, defeated one of the AMFm's core objectives of increasing affordability of ACTs (The Global Fund, 2009b). In this paper we explored factors influencing two levels of adherence to the RRP: stocking some co-paid QAACTs at RRP and stocking all available co-paid at RRP.

The survey respondent knowing there was a RRP for the QAACTs with the logo and being able to correctly specify it to be USD 0.96 was our main predictor for the pricing outcomes, and we refer to this simply as “knowledge”. Although the RRP was set by the Ghana AMFm Coordinating Committee, the figure was arrived at in close consultation with the private for-profit sector. In contrast to Resale Price Maintenance and other legal approaches to price maintenance, a key feature of a Recommended Retail Price is that the retailer is not obliged to adhere to it (Mathewson & Winter, 1998; Puppe & Rosenkranz, 2011). One way recommend retail pricing is believed to act, is by influencing the behavior of both retailers and consumers. Based on the assumption that consumers suffer from “loss aversion”, RRP based on good market intelligence contribute to setting some kind of reference point or ceiling of consumers’ willingness to pay (Kahneman, Knetsch, & Thaler, 1991; Tversky & Kahneman, 1991). Research shows that even monopolistic retailers voluntarily adhere to the RRP when they are concerned that consumer’s exercise of personal agency in purchasing an antimalarial (influenced by their awareness of the RRP), might be lower than the price the retailer would have otherwise set (Puppe & Rosenkranz, 2011). Thus for RRP to be effective, achieving high levels of awareness for both consumers and retailers is critical, especially considering that the RRP for co-paid QAACTs was not printed on the packaging.

Empowering key actors with knowledge has been shown to be critical for the successful implementation of various malaria control interventions (B. P. Kangwana et al., 2013). Knowledge is able to induce action/compliance, whether it be using ACTs, adhering to a treatment regimen, or purchasing and sleeping under bed nets (Aborah et

al., 2013; Wafula et al., 2012). There is convincing evidence that the level of knowledge of the RRP was a direct outcome of the intensity and extent of communication campaigns to boost both retailer and consumer awareness, and that knowledge translated into retailer adherence to the RRP (Tougher et al., 2012; Willey et al., 2014). In Ghana, over 10,000 radio spots and 400 television commercials were aired in English and 7 other local languages, and training on the AMFm was administered to providers across the health sector (AMFm IE Team, 2012). In Ghana and other AMFm countries where the green-leaf logo identifying the co-paid QAACTs and the RRP was widely promoted, knowledge of the RRP among retailers was found to be high (84% in Ghana) (J. Amuasi et al., 2012; Willey et al., 2014). From a qualitative study, this high level of knowledge corresponded with a very narrow interquartile price range for co-paid QAACT prices and a median price just below the RRP (Willey et al., 2014).

The hypothesis of a relationship between knowledge and adherence to the RRP is further supported by our findings showing awareness of the RRP and correctly specifying it (knowledge), to be a strong independent predictor of stocking some or all co-paid QAACTs at RRP ($p < 0.001$ for both). However the difference in predicted probability of stocking some co-paid QAACTs at RRP between those who had knowledge and those who did not was 49%, while for those outlets stocking all at RRP, the difference was 26%. The “difference-in-differences” of 23 percentage points, and the evidence of other independent predictors of adherence to the RRP, indicates that aside from knowledge, there are other important factors to consider if improvements in adherence to the RRP are desired. A yet-to-be-published report examining the AMFm data from a number of pilot

countries also suggests that there is potential for further reductions in price if greater adherence to the RRP is achieved (Tougher et al, in press).

Compared to outlets in low prevalence areas, we hypothesized that outlets in areas of high malaria prevalence would be more likely to stock QAACTs due to a greater demand for antimalarials and that these outlets would be more likely to sell QAACTs at the RRP due to the higher levels of poverty among populations in high prevalence, often rural, regions. Previous analyses on the association between malaria prevalence and QAACT pricing during the AMFm have shown mixed results. An analysis of remote regions of Tanzania during the first year of the AMFm found that towns with lower malaria prevalence had slightly higher prices of co-paid QAACTs than high prevalence towns (Yadav et al., 2012). On the other, an analysis 3 months after the launch of the AMFm in Kenya found no correlation between the incidence of fever and ACT stocking and pricing (O'Meara et al., 2013). In our analysis,

We observed the hypothesized positive association between Pfpr and stocking some co-paid QAACTs at RRP manifesting only after adjusting for knowledge, number of co-paid QAACTs audited, and the kinds of active ingredients stocked ($p=0.013$). After confirming the absence of multicollinearity between Pfpr and the other predictors in our multivariate regression model, we conclude that the association between Pfpr and stocking some co-paid QAACTs at the RRP was being “negatively confounded” by knowledge (MacKinnon, Krull, & Lockwood, 2000). We have already established that lower levels of knowledge are associated with lower levels of stocking at RRP independent of Pfpr. Further analysis (not captured in our results section), shows that

high Pfpr is strongly associated with lower levels of knowledge relative to low Pfpr ($p=0.003$). Higher Pfpr is often associated with lower wealth quintiles, which further lowers the probability of ownership of radios or televisions and by extension exposure to information on the AMFm. Therefore by adjusting for knowledge, the positive association between Pfpr and stocking some co-paid QAACTs at RRP becomes evident.

Our results showed that with increasing number of co-paid QAACTs in an outlet, the probability that some would be stocked at RRP increased, while the probability that all would be stocked at RRP decreased. The number of co-paid QAACTs and the type being stocked (ASAQ or AL, adult or pediatric) in an outlet were important factors associated with whether or not an outlet stocked some or all its co-paid QAACTs at RRP. The importance of the number and type of co-paid QAACTs in an outlet in relation to stocking at the RRP is highlighted when we consider that 34% of our sample (184 outlets) stocked only 1 co-paid QAACT. Out of these 184 single co-paid QAACT-stocking outlets, 73% of 158 and 35% of 26 stocked AL and ASAQ respectively at the RRP (21% and 2% of our sample respectively). See Appendix 18 and 19 for further details. Further analysis (see Appendix 20) shows that the median prices per AETD of co-paid ASAQ and AL in our sample were different at USD 1.25 and USD 0.94 respectively ($p=0.004$). It is therefore not surprising that overall, stocking AL only led to a higher predicted probability of stocking some or all co-paid QAACTs at RRP than stocking ASAQ only, and a higher predicted probability of stocking all at RRP than stocking both ASAQ and AL.

Going beyond the outlet level analyses to examine the distribution of the antimalarials themselves, we find that of all the co-paid QAACTs that were ASAQ (428), 29% were pediatric formulations, whereas out of all the co-paid QAACTs that were AL (1,018), only 17% were pediatric. Also, out of the 294 pediatric co-paid QAACTs, 42% were ASAQ and the rest were AL, whereas out of the 1,152 adult co-paid QAACTs, only 26% were ASAQ and the rest were AL. These findings indicate that although there was much more AL than ASAQ stocked in the private sector (70% vs. 30%), there was a bias in favor of adult formulations for AL and pediatric formulations for ASAQ. These phenomena are likely to be a reflection of existing consumer preferences, which have been observed and echoed by the National Malaria Control Program (J. Amuasi, 2013).

Our results showed that for both ASAQ and AL, AETDs of pediatric co-paid QAACTs were mostly sold above the RRP. This is not surprising, considering that a number of pediatric treatment packs have to be combined to achieve an adult equivalent treatment dose (AETD), which has the potential to bias the price of the AETD upwards, as opposed to a straight adult treatment pack. A lot of the research on pricing of antimalarials therefore separates the analysis of adult treatments from pediatric treatments. Further, because markets generally have higher volumes of adult treatments, many antimalarial pricing studies focus only on adult treatments to achieve greater statistical power. However we believe that analyzing adult and pediatric treatments together and adjusting for the influence of their distribution is a better policy-oriented approach to pricing studies than separate analyses or outright exclusions.

We see from this study that outlets sometimes stock only adult or pediatric treatment packs. In such situations, adult customers are compelled to achieve the required treatment dose by either adding up a number of pediatric treatment packs to make up an adult equivalent treatment dose (AETD), or dividing an adult pack to achieve a pediatric dose. In this regard, capturing the influence of the adult/pediatric distribution in this pricing study allows us to better translate our results into realistic policy recommendations based on the prevailing scenario in the antimalarial market. The higher average cost per AETD of pediatric formulations and the finding that pediatric formulations were more biased towards ASAQ than AL, accounts for the observed higher median price of ASAQ compared to AL.

Notwithstanding the importance of our findings, we must acknowledge there are a number of important limitations to this study. First, the pricing information we are using was collected as part of the AMFm IE, and was obtained from retailer's responses to questions posed by data collectors. Although likely to be much more costly, to avoid issues associated with self-reporting (B. P. Kangwana et al., 2013), we recommend that subsequent pricing studies consider employing mystery shopping as the approach to collecting information on antimalarial prices.

Second, competition is known to often be an important influencer of medicine prices. However we cannot include any relevant measure of competition using our data because of the cluster sampling approach used for data collection.

Third, in studying the private-for-profit sector, owing to sample size limitations our study does not make any distinction among stand-alone pharmacies, pharmacies

attached to private health facilities, licensed chemical shops and itinerant vendors. While the private sector is arguably fairly homogeneous, several unmeasured factors (e.g. the high concentration of pharmacies in urban areas in Ghana) (F. Smith, 2004), could influence our findings in ways potentially important for policy considerations.

Finally, the data collected focuses only on retailer behavior and not on consumer's behavior. Considering that the impact of the AMFm subsidy is a function of the interaction between retailers and consumers, we could be missing some valuable information which could enrich our understanding of the observed phenomena and help refine recommended policy actions. Future studies on the impact of price subsidy interventions such as the AMFm on antimalarial availability, pricing and use should therefore include consumer exit interviews.

In spite of these limitations, the strengths of our data and analyses far outweigh any weaknesses. This study has shown that retailer's adherence to the RRP for co-paid QAACTs can be high when knowledge is made available to both consumers and retailers. The RRP was set by the Ghana AMFm Coordinating Committee in consultation with key stake-holders, including the private sector, which provided various estimates of costs at various stages of their supply chain. Therefore information asymmetry between the private sector actors in the supply chain and the rest of the policy makers who decided on the RRP, could have resulted in an inflated RRP. An inflated RRP might have resulted in unfair profits for retailers and prevented customers from experiencing the full potential benefit of the subsidy.

Since specifying a RRP inadvertently sets a price floor (AMFm IE Team, 2012), we recommend that careful consideration continue to be given to the level at which the RRP is set so that it resonates with both consumers' willingness to pay and fair profits for retailers. While printing the RRP on the packaging could be a powerful tool for modifying market forces, it risks creating more confusion, considering the instability of the Ghana Cedi relative to the US Dollar, the wide range of QAACT formulations available, and the shelf-life of ACTs.

We also recommend that information on the AMFm subsidy be disseminated with greater focus on those areas of high malaria prevalence such as the northern savanna zone. Innovative ways of delivering information on the subsidy tailored specifically to these high Pfpr areas is more likely to increase awareness of the availability and RRP of the co-paid QAACTs than more generalized approaches.

Finally, Dihydroartemisinin-Piperaquine (DHAP) is an ACT that has been included as an alternative first-line therapy for treating uncomplicated malaria in Ghana, and is used mainly by adults (Abuaku, Duah, Quaye, Quashie, & Koram, 2012), and is likely to soon attain QAACT status (EMEA, 2012). We therefore recommend that the Ministry of Health in Ghana consider initiating steps to improve the popularity of DHAP among consumers. Increased knowledge about the relatively newer drug should lead to an increase in demand for it, and an increase in competition between DHAP and AL for use among adults, eventually driving both prices down.

The above must be followed by the Ministry of Health adopting policies supporting the use of ASAQ for children and AL or DHAP for adults for the treatment

uncomplicated malaria. Our findings and other sources indicate that this population segmentation approach to multiple first-line antimalarial therapy is already the *de-facto* situation in Ghana (J. Amuasi, 2013). By taking advantage of a situation that has already been created naturally by market forces, the message on co-paid QAACTs and their importance for treatment of uncomplicated malaria can be reinforced to allow for even better compliance with RRP.

Any policy change should be coupled with monitoring of prices and other indicators in the market in order to accurately measure the effects of the interventions over time, and monitoring of resistance to ACTs.

Table 7: Unweighted distribution of outlet characteristics

Characteristics		Stocked co-paid QAACTs	Stocked some co-paid QAACTs at RRP	Stocked all co-paid QAACTs at RRP
<i>Total: N, %</i>		<i>545, 100%</i>	<i>412, 100%</i>	<i>173, 100%</i>
Respondent knew and specified the RRP for co-paid QAACTs		86.8	93.9	91.3
Stocked at least 1 co-paid QAACT that was ASAQ		46.2	46.6	16.2
Stocked at least 1 co-paid QAACT that was AL		92.8	96.4	94.8
Stocked at least 1 oral AMT		56.7	57.8	46.2
Stocked at least 1 nAT*		54.1	54.6	52.6
Stocked at least 1 non-AMFm QAACT		27.5	28.2	12.7
Stocked at least 1 non-QAACT		81.3	83.3	71.7
Respondent owned the outlet		35.1	35.9	44.5
Malaria testing (microscopy/RDT) available		4.8	4.4	2.9
At least 1 employee completed secondary/high school		94.3	95.2	91.3
At least 1 employee is a pharmacist, nurse or doctor		56.7	58	44.5
Number of employees**	<i>One</i>	<i>13</i>	<i>13.6</i>	<i>22</i>
	<i>Two</i>	<i>33.9</i>	<i>32.3</i>	<i>41</i>
	<i>Three</i>	<i>22.6</i>	<i>22.6</i>	<i>19.7</i>
	<i>Four or more</i>	<i>30.3</i>	<i>30.3</i>	<i>17.3</i>
Number of co-paid QAACTs audited	<i>One</i>	<i>33.8</i>	<i>30.4</i>	<i>72.2</i>
	<i>Two-Three</i>	<i>40.5</i>	<i>40.5</i>	<i>27.2</i>
	<i>Four or more</i>	<i>25.7</i>	<i>29.2</i>	<i>0.6</i>
Active ingredients of co-paid QAACTs	<i>ASAQ only</i>	<i>7.2</i>	<i>3.6</i>	<i>5.2</i>
	<i>AL only</i>	<i>53.8</i>	<i>53.4</i>	<i>83.8</i>
	<i>Both ASAQ and AL</i>	<i>39</i>	<i>43</i>	<i>11</i>
Formulation of co-paid QAACTs	<i>Adult only</i>	<i>55.8</i>	<i>55.8</i>	<i>97.7</i>
	<i>Pediatric only</i>	<i>2.4</i>	<i>0</i>	<i>0</i>
	<i>Both Adult and Pediatric</i>	<i>41.8</i>	<i>44.2</i>	<i>2.3</i>
Geographic area	<i>Urban</i>	<i>76.7</i>	<i>77.2</i>	<i>66.5</i>
	<i>Rural</i>	<i>23.3</i>	<i>22.8</i>	<i>33.5</i>
Malaria epidemiologic zone [§]	<i>Coastal savanna/Mangrove swamps</i>	<i>50.4</i>	<i>49.5</i>	<i>39.9</i>
	<i>Tropical rain forest</i>	<i>38.2</i>	<i>39.3</i>	<i>42.2</i>
	<i>Northern savanna</i>	<i>11.4</i>	<i>11.2</i>	<i>17.9</i>
<i>Falciparum</i> malaria prevalence (%)	<i>Low (10-24)</i>	<i>35.8</i>	<i>35.4</i>	<i>22.5</i>
	<i>Medium (25-34)</i>	<i>34.5</i>	<i>35.4</i>	<i>39.9</i>
	<i>High (35-70)</i>	<i>29.7</i>	<i>29.2</i>	<i>37.6</i>

*Excludes SP, Quinine, and those antimalarials used strictly for prophylaxis or no longer for treatment

**Percentages may not add up to 100% because of rounding or missing data

[§]Approximation based on demarcations of ecological zones (Coastal, Forest and Northern) used by the Ghana Statistical Service

AETD: Adult Equivalent Treatment Dose

QAACT: Quality Assured Artemisinin-based Combination Therapy

RDT: Rapid Diagnostic Test for malaria

RRP: Recommended Retail Price

Table 8: Survey weighted means of continuous variables by outcomes

Variables	Some co-paid QAACTs sold at RRP			All co-paid QAACTs sold at RRP		
	mean (95%CI)		p-value	mean (95%CI)		p-value
	Yes n=412	No n=133		Yes n=173	No n=372	
<i>Falciparum</i> malaria prevalence (percent)	32.5 (27.9, 37.1)	33.7 (28.8, 38.5)	0.451	35.5 (31.1, 39.9)	31.1 (26.5, 35.7)	*0.001
Number of employees	2.6 (2.4, 2.8)	2.4 (2.2, 2.7)	0.34	2.2 (2, 2.4)	2.7 (2.5, 2.9)	*0.001
Number of co-paid QAACTs audited	2.4 (2.2, 2.6)	1.9 (1.6, 2.1)	*<0.001	1.3 (1.2, 1.4)	2.9 (2.7, 3.1)	*<0.001
Sales volume of all antimalarials (in AETDs. Mean, 95% CI)	69.2 (53.4, 84.9)	34.5 (20.1, 48.9)	*<0.001	47.2 (37.3, 57)	68.5 (48.3, 88.6)	0.050
Sales volume of co-paid QAACTs (in AETDs. Mean, 95% CI)	37.8 (29.6, 46.1)	13.8 (8.6, 19)	*<0.001	27.7 (20.1, 35.3)	34.2 (25.2, 43.2)	0.242
Relative sales volume of co-paid QAACTs (in percent. Mean, 95% CI)	58.4 (55, 61.9)	51.4 (42.7, 60.1)	0.119	57.1 (51.6, 62.5)	56.6 (52.6, 60.6)	0.886
<i>P-values were derived from t-tests of significance for differences between the response categories "Yes" and "No" in the survey weighted mean of each variable</i>						
<i>*Statistically significant p-value (≤ 0.05)</i>						
<i>AETD: Adult Equivalent Treatment Dose</i>						
<i>QAACT: Quality Assured Artemisinin-based Combination Therapy</i>						
<i>RRP: Recommended Retail Price</i>						

Table 9: Survey weighted mean *falciparum* malaria prevalence among outlet locations by pricing outcomes

		Falciparum malaria prevalence (%)			
Variables		Some co-paid QAACTs sold at RRP (n=412/545)		All co-paid QAACTs sold at RRP (n=173/545)	
		mean (95% CI)	p-value	mean (95% CI)	p-value
Location	Rural	39.3 (34.5, 44)	*0.014	40.7 (36.1, 45.3)	*0.038
	Urban	29.7 (23.7, 35.6)		32.3 (25.9, 38.8)	
Malaria epidemiologic zone [§]	Coastal savanna/Mangrove swamps	22.6 (17.1, 28)	*0.001	25 (18.5, 31.5)	*<0.001
	Tropical rain forest	34.7 (31, 38.4)		34.6 (31.3, 37.9)	
	Northern savanna	54.1 (50.5, 57.7)		54.4 (51, 57.8)	

P-values were derived from t-tests of significance for differences between the categories for the variables in the survey weighted mean malaria prevalence

**Statistically significant p-value (≤ 0.05)*

§Approximation based on demarcations of ecological zones (Coastal, Forest and Northern) used by the Ghana Statistical Service

RRP: Recommended Retail Price

Table 10a: Survey weighted percentages of outlets with the pricing outcomes

Characteristics		Some co-paid QAACTs sold at RRP		All co-paid QAACTs sold at RRP	
		w%	p-value	w%	p-value
<i>N=545</i>					
Respondent knew and specified the RRP for co-paid QAACTs	Yes	82.9	* <0.001	40.8	*0.008
	No	32.5		23.1	
Malaria testing (microscopy/RDT) available	Yes	61.7	0.104	27.3	0.185
	No	74.9		38.3	
Respondent owned the outlet	Yes	77.9	0.173	44.6	*0.002
	No	72		32.2	
At least 1 employee completed secondary/high school	Yes	75.7	0.132	36.9	0.128
	No	66.3		50.5	
At least 1 employee is a pharmacist, nurse or doctor	Yes	76.3	0.339	31.5	*0.009
	No	73		42.5	
Number of employees	One	79.7	0.423	58.1	* <0.001
	Two	72.1		39	
	Three	76.1		29.2	
	Four or more	76.2		23.4	
Location	Rural	70.5	0.280	46.0	*0.047
	Urban	76.6		34.2	
Malaria epidemiologic zone [§]	Coastal savanna/Mangrove swamps	73.6	0.926	30.4	*0.001
	Tropical rain forest	75.6		39	
	Northern savanna	74.8		56.4	
<i>Falciparum</i> malaria prevalence (%)	Low (10-24)	75.0	0.722	25.7	*0.008
	Medium (25-34)	76.6		42.8	
	High (35-70)	72.8		42.6	

P-values were derived from χ^2 tests of significance of the differences in adjusted survey weighted predicted probabilities of the outcomes for the categories of each variable. "Yes", "One", "Rural", "Coastal savanna", and "Low" were reference groups

**Statistically significant p-value*

§Approximation based on demarcations of ecological zones (Coastal, Forest and Northern) used by the Ghana Statistical Service

QAACT: Quality Assured Artemisinin-based Combination Therapy

RDT: Rapid Diagnostic Test for malaria

RRP: Recommended Retail Price

Table 10b: Survey weighted percentages of outlets with the pricing outcomes (for antimalarial stocking-related variables)

Antimalarial stocking characteristics		Some co-paid QAACTs sold at RRP		All co-paid QAACTs sold at RRP	
		w%	p-value	w%	p-value
N=545					
Active ingredients of co-paid QAACTs	<i>ASAQ only</i>	46.7		24.8	
	<i>AL only</i>	74.6	* <i><0.001</i>	55.8	* <i><0.001</i>
	<i>Both ASAQ and AL</i>	81.3		11.7	
Formulation of co-paid QAACTs [§]	<i>Adult only</i>	74.8		59.2	
	<i>Both Adult and Pediatric</i>	78.8	0.294	2.4	* <i><0.001</i>
Number of co-paid QAACTs audited	<i>One</i>	69.3		69.3	
	<i>Two-Three</i>	74.9	* <i>0.011</i>	24.4	* <i><0.001</i>
	<i>Four or more</i>	85.3		0.3	
Stocked oral AMTs	<i>Yes</i>	76.4		29.6	
	<i>No</i>	73	0.370	46.3	* <i><0.001</i>
Stocked at least 1 non-AMFm QAACT	<i>Yes</i>	80.1		21.7	
	<i>No</i>	73.8	0.179	40.5	* <i>0.001</i>
Stocked at least 1 non-QAACT	<i>Yes</i>	77		34.3	
	<i>No</i>	68.5	* <i>0.040</i>	47.5	* <i>0.007</i>
Stocked at least 1 nAT**	<i>Yes</i>	76.2		35.4	
	<i>No</i>	72.6	0.321	41.1	0.090

P-values were derived from χ^2 tests of significance of the differences in adjusted survey weighted predicted probabilities of the outcomes for the categories of each variable. "Yes", "ASAQ only", "Adult only" and "One" were reference groups

**Statistically significant p-value*

§"Pediatric only" excluded because no outlet that stocked only pediatric co-paid QAACTs sold any at RRP

***Excludes SP, Quinine, and those antimalarials used strictly for prophylaxis or no longer for treatment*

QAACT: Quality Assured Artemisinin-based Combination Therapy

AMT: Artemisinin Monotherapy

nAT: non-Artemisinin Therapy

RRP: Recommended Retail Price

ASAQ: Artesunate-Amodiaquine

AL: Artemether-Lumefantrine

Table 11: Adjusted probability of stocking some co-paid QAACTs at RRP

Characteristics		Some co-paid QAACTs sold at RRP N=545	
		<i>Pr</i>	<i>p-value</i>
Respondent knew and specified the RRP for co-paid QAACTs	<i>Yes</i>	82.1	<i>*<0.001</i>
	<i>No</i>	33.1	
<i>Falciparum</i> malaria prevalence (%)	<i>Low (10-24)</i>	68.1	<i>*0.013</i>
	<i>Medium (25-34)</i>	74.3	
	<i>High (35-70)</i>	77.9	
Active ingredients of co-paid QAACTs	<i>ASAQ only</i>	56.2	<i>*0.014</i>
	<i>AL only</i>	76.8	
	<i>Both ASAQ and AL</i>	76.9	
Number of co-paid QAACTs audited	<i>One</i>	71.8	0.082
	<i>Two-Three</i>	74.1	
	<i>Four or more</i>	82.6	

P-values were derived from χ^2 tests of significance of the differences in adjusted survey weighted predicted probabilities of the outcome for the categories of each variable. "Yes", "Low", ASAQ only", and "One" were reference groups

**Statistically significant p-value (≤ 0.05)*

QAACT: Quality Assured Artemisinin-based Combination Therapy

RRP: Recommended Retail Price

Table 12: Adjusted probability of stocking all co-paid QAACTs at RRP

Characteristics		All co-paid QAACTs sold at RRP N=545	
		<i>Pr</i>	<i>p-value</i>
Respondent knew and specified the RRP for co-paid QAACTs	<i>Yes</i>	43.9	<i>*<0.001</i>
	<i>No</i>	18	
Respondent owned the outlet	<i>Yes</i>	40.6	0.217
	<i>No</i>	37	
At least 1 employee is a pharmacist, nurse or doctor	<i>Yes</i>	40.9	0.302
	<i>No</i>	37.4	
Number of employees	<i>One</i>	45.5	0.272
	<i>Two</i>	37.3	
	<i>Three</i>	38	
	<i>Four or more</i>	34.5	
Active ingredients of co-paid QAACTs	<i>ASAQ only</i>	27.6	<i>*0.005</i>
	<i>AL only</i>	42.6	
	<i>Both ASAQ and AL</i>	31	
Formulation of co-paid QAACTs [§]	<i>Adult only</i>	46.8	<i>*<0.001</i>
	<i>Both Adult and Pediatric</i>	8.7	
Number of co-paid QAACTs audited	<i>One</i>	48.2	<i>*<0.001</i>
	<i>Two-Three</i>	32.6	
	<i>Four or more</i>	2.3	
Location	<i>Rural</i>	40.2	0.582
	<i>Urban</i>	37.9	
Malaria epidemiologic zone**	<i>Coastal savanna/Mangrove swamps</i>	38.4	0.877
	<i>Tropical rain forest</i>	38.2	
	<i>Northern savanna</i>	40.9	
<i>Falciparum</i> malaria prevalence (%)	<i>Low (10-24)</i>	34.1	0.238
	<i>Medium (25-34)</i>	39.8	
	<i>High (35-70)</i>	40.3	

P-values were derived from χ^2 tests of significance of the differences in adjusted survey weighted predicted probabilities of the outcome for the categories of each variable. "Yes", "One", "ASAQ only", "Adult only", "Rural", "Coastal savanna", and "Low" were reference groups

**Statistically significant p-value (≤ 0.05)*

§ "Pediatric only" excluded because no outlet that stocked only pediatric co-paid QAACTs sold any at RRP

***Approximation based on demarcations of ecological zones (Coastal, Forest and Savanna) used by the Ghana Statistical Service*

QAACT: Quality Assured Artemisinin-based Combination Therapy

RRP: Recommended Retail Price

Table 13: Survey weighted relationship between number of co-paid QAACTs and proportion at RRP

Proportion (%) of co-paid QAACTs at RRP	Number of co-paid QAACTs in an outlet			TOTAL, (N = 545)
	One (n=184)	Two-Three (n=221)	Four or more (n=140)	
None, n=133	30.7%	25.1%	14.7%	25.3%
12.5 - 44.4, n=86	0	12.9%	33.2%	11.6%
50, n=89	0	28.1%	27.8%	16.7%
55.6 - 80, n=64	0	9.5%	24.1%	8.5%
All, n=173	69.3%	24.4%	0.3%	37.9%
TOTAL, (N = 545)	100%	100%	100%	100%

χ^2 test p-value <0.001 (8 df)

QAACT: Quality Assured Artemisinin-based Combination Therapy

RRP: Recommended Retail Price

Chapter 5: The Impact of Training on Knowledge of the Recommended Retail Price for AMFm Co-paid Antimalarials in Urban and Rural Outlets in Ghana

Introduction

Even though the World Health Organization (WHO) has recommended artemisinin-based combination therapies (ACTs) as first-line treatment for uncomplicated *P. falciparum* malaria, they remain relatively expensive and largely unaffordable to the rural poor, who are both more susceptible to getting malaria and often face challenges accessing antimalarial outlets. Malaria stakeholders therefore created the Affordable Medicines Facility – malaria (AMFm), which was piloted in 7 countries including Ghana between 2010 and 2013, as a financing mechanism for quality-assured ACTs (QAACTs), which had a relatively low recommended retail price tag (RRP). The AMFm involved price negotiations with manufacturers, subsidies, and supporting interventions (SIs).

Retailer awareness of the RRP and correctly specifying it (knowledge) has been shown to be a strong independent predictor of stocking QAACTs at the RRP. The AMFm objectives were increasing affordability, availability, market-share, and use of QAACTs. Creation of knowledge about the AMFm intervention and the RRP for the co-paid QAACTs was an important intermediary outcome of the SIs accompanying its implementation in Ghana. Using data from the independent evaluation (IE) of the AMFm, we employed survey weighted multivariate logistic regression techniques to explore differences between urban and rural outlets in the association between exposure to training and knowledge of the RRP for co-paid QAACTs in private-for-profit outlets.

Among outlets in rural locations, the odds of having knowledge of the RRP was 10.23 times higher for outlets with at least one AMFm trained employee compared to those with none ($p<0.001$). On the other hand, for outlets without any AMFm trained employees, the odds of having knowledge of the RRP was 9.53 times higher for outlets in urban locations compared to those in rural areas (the reference category) ($p<0.001$). The similarity of these two odds ratios (10.23 and 9.53) indicates that training raises outlets in rural locations to an odds ratio of having knowledge of the RRP equivalent to that of outlets in urban locations that had not undergone any training (rural untrained outlets as reference group). Our computations further showed the marginal impact of training for rural outlets as increasing the probability of knowledge by 46% ($p<0.001$), while for urban outlets it was only 4.8% ($p=0.208$). Thus knowledge of the RRP as an outcome of having received training was particularly important for rural outlets. In contrast, the impact of training on knowledge among urban outlets was much less impressive. We believe that this difference is due to there being many other sources of knowledge of the AMFm beyond training, especially in urban areas, allowing less room for improvement in knowledge with training in urban areas compared to rural areas.

Based on these findings and estimates of malaria cases per outlet across malaria epidemiologic zones in Ghana, we recommend that in addition to increasing the proportion of retailers trained and intensifying other SIs in high prevalence and rural areas, ongoing measures aimed directly at increasing access to outlets and driving down the case-outlet ratio are intensified. These measures include building of Community-

based Health Planning and Services compounds, promoting the use of long lasting insecticide treated nets, and carrying out indoor residual spraying.

Background

Malaria continues to be a major public health concern in Ghana. Transmission occurs year round, with peaks during the rainy season. Though there is risk of malarial in all regions of the country, infection rates are higher in rural than in urban areas. Public sector health facility data show that malaria accounts for 38.2% of all outpatient illnesses, 34.9% of all admissions, and 33.7% of all deaths in children under 5 years old (NMCP, 2010). Data from the public healthcare sector reflects a small fraction of actual malaria infections, since about 60% of the population access treatment from the private for-profit sector, particularly from pharmacies and licensed chemical shops (Adeyi & Atun, 2010; Buabeng et al., 2010; PMI, 2011; RBM Partnership, 2013).

Socioeconomic factors (which also affect the urban poor) (WHO, 2010a), often limit access to prompt treatment in rural areas, compounded by the fact that more health outlets are located in urban areas (GSS and ICF Macro, 2009). This combination means that the rural poor are both more susceptible to getting malaria, and less able to access and afford effective treatment (Worrall et al., 2005).

Since 2001, the World Health Organization (WHO) has recommended artemisinin-based combination therapies (ACTs) as first-line treatment for uncomplicated *P. falciparum* malaria (WHO, 2006). Ghana's current antimalarial policy includes three ACTs: Artesunate-Amodiaquine (ASAQ), Artemether-Lumefantrine (AL) and Dihydroartemisinin-Piperaquine (DHAP) as recommended first-line therapies for the treatment of uncomplicated malaria (MoH, 2009a). Even though the WHO recommends ACTs for the treatment of uncomplicated malaria, their high cost relative to less-effective

medicines remains a major barrier to access. The Affordable Medicines Facility – malaria (AMFm), hosted by The Global Fund to Fight AIDS Tuberculosis and Malaria, was a financing mechanism for quality-assured ACTs (QAACTs) involving price negotiations with manufacturers, subsidies, and supporting interventions (SIVs). The AMFm was designed to increase affordability, availability, market-share, and use of QAACTs. Between 2010 and 2013, the AMFm was piloted in 7 countries including Ghana, where its outcomes were measured and evaluated by an Independent Evaluation (IE) team (Tougher et al., 2012).

The AMFm IE in Ghana showed significant increases in QAACT market share in the private-for-profit sector between baseline and endline surveys (from 6.5% to 51.8% of all antimalarials sold/distributed in the week preceding the survey). This increase was similar for rural and urban areas. However, both recognition of the AMFm green-leaf logo and knowledge of the recommended retail price (RRP) for QAACTs were higher in urban outlets than in rural ones (AMFm IE Team, 2012; J. Amuasi et al., 2012). Despite these patterns, at endline, the AMFm IE in Ghana found no differences in outlets having at least one staff member that received training on co-paid QAACTs between urban and rural areas. However at endline, more private-for-profit outlets in urban than rural areas (45% vs. 21%) had an employee with a health-related qualification (pharmacy, nurse or medical doctor related training).

An important intermediary outcome of the country roll-out of AMFm SIVs was the creation of knowledge about the AMFm intervention and the RRP for the co-paid QAACTs (see Figure 3: Conceptual Model). The hypothesized relationship between

knowledge and adherence to the RRP is supported by findings that awareness of the RRP and correctly specifying it (knowledge), was a strong independent predictor of stocking some or all co-paid QAACTs at RRP ($p < 0.001$ for both) (Amuasi et al., unpublished manuscript).

Of the 24.7 million co-paid QAACTs delivered to Ghana within the AMFm evaluation period, 95% were purchased by private for-profit first-line buyers (wholesalers). The private for-profit sector was responsible for at least two-thirds of all antimalarials sold or distributed at baseline and endline, with a higher market share of QAACTs at endline in urban areas than in rural areas (76% vs. 57%). These findings confirm the importance of the private sector in malaria control, and reflect the positive impact that the AMFm had on the antimalarial delivery system in Ghana. The private health sector is much larger and more complicated than the public sector, resulting in different kinds of challenges with regard to making ACTs accessible.

Comparing sectors for changes in QAACT availability, the largest rise in QAACT availability was seen in private for-profit outlets (from 24.8% of outlets at baseline to 82.6% at endline stocking at least one QAACT). Between baseline and endline, QAACT availability also increased proportionately more in rural than in urban areas (by 58 vs. 38 percentage points). This difference resulted in a reduction in the urban-rural gap in QAACT availability at baseline from 28.3 percentage points, to 10.8 percentage points at endline (AMFm IE Team, 2012).

Irrespective of the disease/condition of interest, age group, or economic standing of a country, rural/urban differences in access to health services persist (Fotso, 2006;

Kozhimannil, Hung, Prasad, Casey, & Moscovice, 2014; Moscovice & Casey, 2009; Strasser, 2003; Virnig, Ma, Hartman, Moscovice, & Carlin, 2006). Recognizing and understanding their underlying causes is therefore critical to improving outcomes from interventions (WHO, 2010a).

In this paper, we explore differences between urban and rural outlets in the impact of training on knowledge of the recommended retail price for co-paid QAACs in private-for-profit outlets. We also discuss the malaria control policy implications of our findings.

Methods

Data Source

We used data collected as part of the AMFm IE endline survey in Ghana carried out in 2011. The IE took into account the well-known malaria prevalence and socio-economic disparities between rural and urban areas by calculating sample sizes separately for urban and rural domains (Tougher et al., 2012). A multi-phase cluster sampling approach was adopted with a predetermined number of geographic clusters selected with probability proportional to size. Other sources describe the unique IE sampling approach in Ghana, data collection, and analysis process in detail (J. Amuasi et al., 2012; Tougher et al., 2012).

Data on *Plasmodium falciparum* malaria prevalence by district were obtained from the 2010 posterior predictive distribution model estimates produced by the Malaria Atlas Project (MAP). Shapefiles and other geographic information systems data on

districts in Ghana were obtained from the Centre for Remote Sensing and Geographic Information Services of the University of Ghana via ESRI's GeoCommons platform (CERSGIS, 2012).

The University of Minnesota Institutional Review Board (IRB) determined that our study was using secondary data, did not meet the regulatory definition of research with human subjects, and so did not require additional IRB clearance. Prior to the IE data collection in Ghana, IRB clearance was obtained from the Ghana Health Service Ethical Review Committee on Research Involving Human Subjects (ERCRIHS).

Data Management

The Ghana IE endline survey dataset comprise information on 765 private sector outlets and a total of 6,117 antimalarial products. All outlets that were enumerated and completed the interview were included in our study, irrespective of whether or not they stocked antimalarials. A total of 117 outlets were excluded from the sample because they fell into either of the following categories: 1) Were not screened, 2.) Did not meet the screening criteria, 3) Were not interviewed, 4) Did not fully complete the interview and antimalarial audit, and 5) Were private not-for-profit facilities.

The endline survey data on outlet location was layered on the map of Ghana districts using ArcMap v10.2 (ESRI, 2013). The data on *Plasmodium falciparum* malaria prevalence by district was extracted from the MAP database and merged with the endline survey data using the “spatial join” feature in ArcMap.

Variables

Knowledge of the RRP for the QAACTs with the AMFm logo and being able to correctly specify it to be USD 0.96 was our outcome of interest. The primary predictors included in our analysis were whether at least one employee of the outlet had received training on co-paid QAACTs at endline, and whether the outlet was in an urban or rural location.

We included other potentially confounding outlet characteristics as independent variables in our analyses. These included type of outlet (pharmacy or licensed chemical shop), *Falciparum* malaria prevalence (Pfpr - low, mid or high category), and the category of malaria epidemiologic zone within which the outlet was located. The availability of malaria testing, completion of secondary school of at least 1 employee, and having a pharmacist, nurse or doctor on staff, were also included to account for the outlet's level of sophistication. We also used number of workers employed in the outlet as a measure of outlet size.

Statistical Approach

We used multivariate logistic regressions to assess the association of exposure to training and urban/rural location with knowledge of the RRP, restricted to the private-for-profit sector. We included an interaction between training and location to assess whether the association between training and knowledge differed between urban and rural locations. As shown in Table 15, we adjusted/controlled for variables that were statistically significant from our examination of the unadjusted relationships between independent variables and our knowledge outcome.

Odds ratios and predicted probabilities were generated and used to explain the associations between training and knowledge among outlets located in urban and rural areas. In all models, we performed several sensitivity analyses using alternate models, including using different variable categorizations, to confirm that the observed effects were not artifacts. P-values ≤ 0.05 were considered significant. All analyses were carried out using STATA v12 (StataCorp, 2012). For all analyses, we used the IE endline survey weights to account for the complex nature of the survey design.

Results

Private Sector Outlet Characteristics

From the AMFm IE dataset, we identified 648 private for-profit outlets that met our inclusion criteria (86% of all private for-profit outlets that were enumerated) (see Table 14). The sample was composed of near equal numbers of pharmacies and licensed chemical shops (53.7% and 41.8% respectively). Outlets located in urban areas constituted 73.2% of the sample, and 36.6% of the survey respondents were the outlet owners. Outlets with two employees made up almost 40% of the sample, and the mean number of prescribers/dispensers per outlet was 2.2 (95% CI: 2.1, 2.4). Just less than half of the sampled outlets were from the coastal zone (47.8%), while 38.1% and 14% were from the forest and northern savanna zones respectively. At 46%, almost half of the sampled outlets had at least one employee who had received training on the co-paid QAACs. About 84% of the sampled outlets stocked at least 1 co-paid QAAC, and

82% of outlets had a respondent who knew there was a RRP for the co-paid QAACTs and was able to correctly specify it to be USD 0.96 (had knowledge).

Training, Urban/Rural Location and Knowledge

After adjusting for those variables that had a significant unadjusted association with knowledge, training, urban/rural location, and their interaction, remained significantly associated with knowledge. No other variables had significant associations with knowledge in our multivariate model. Nevertheless it is worth noting that an outlet being a pharmacy vs. a licensed chemical shop, and having at least one employee who had completed secondary school, were positively associated with knowledge (OR=1.81, $p=0.162$ and OR=2.03, $p=0.187$ respectively) (see Table 15 and Appendix 21).

Among outlets in rural locations, the odds of having knowledge of the RRP was 10.23 times higher for outlets with at least one AMFm trained employee compared to those with none ($p<0.001$) (see Table 15). On the other hand, for outlets without any AMFm trained employees, the odds of having knowledge of the RRP was 9.53 times higher for outlets in urban locations compared to those in rural areas (the reference category) ($p<0.001$). The similarity of these two odds ratios (10.23 and 9.53) indicates that training raises outlets in rural locations to an odds ratio of having knowledge of the RRP equivalent to that of outlets in urban locations that had not undergone any training (rural untrained outlets as reference group). In contrast, the impact of training on knowledge among urban outlets was much less impressive (also see Appendix 22).

Although not shown in Table 15 (see Appendix 21), we also examined the marginal effect of training on knowledge separately among urban and rural outlets, as the

difference between the predicted probability of having knowledge for outlets with and without at least one AMFm trained employee. We found that rural outlets without training had a predicted probability of knowing the RRP of just under 40% (95% CI: 23%, 55%), while all other combinations of urban/rural and training/no training had a predicted probability of knowing the RRP of over 80%. Urban outlets that had received training had the highest predicted probability of knowing the RRP (89%; 95% CI: 84%, 94%). Our computations showed the marginal impact of training for rural outlets as increasing the probability of knowledge by 46% ($p<0.001$), while for urban outlets it was only 4.8% ($p=0.208$) (see Appendix 23). Again we see knowledge of the RRP as an outcome of having received training, was particularly important for rural outlets. Nevertheless training still had a positive relationship with knowledge among urban outlets.

Malaria prevalence and epidemiologic zones

To determine the number of malaria cases *per annum*, we multiplied population size per cluster by malaria prevalence estimates. We calculated the population/outlet and malaria cases/outlet ratios for a combined sample of public and private sector outlets. We also standardized our computation of number of cases and the case/outlet ratio to the population size of the coastal zone and lowest malaria prevalence category, to produce tables by malaria epidemiologic zone and malaria prevalence category respectively. We restricted these computations to outlets enumerated in clusters only, because a complete census of outlets was conducted only in clusters. For both actual and standardized computations, the population/outlet and cases/outlet ratios increased from coastal through

to the northern savanna zone and from low through to high prevalence area (see figure in Appendix 24 and Tables 16a and 16b).

After adjusting for other covariates in the multivariate model, neither differences in Pfpr level nor malaria epidemiologic zone were associated with knowledge of the RRP ($p=0.342$ and $p=0.885$ respectively). The predicted probability of knowing the RRP was 85% for low Pfpr areas and 75% for both mid- and high Pfpr areas. Stratified by ecological zones, the predicted probability of knowing the RRP was 76%, 79%, and 77% for the coastal, forest and northern savanna zones respectively.

Discussion

Before the turn of the last century, susceptibility to malaria and its negative health outcomes was to a large extent focused on genetic polymorphisms, geographic, and climatic dispositions (Aidoo et al., 2002; Gething et al., 2011). However over the past decade, there has been an increased recognition of the important role socio-economic factors play by themselves or in association with epidemiologic determinants of malaria (J. D. Sachs, Mellinger, & Gallup, 2001; J. Sachs & Malaney, 2002; Worrall et al., 2005). In Ghana, malaria has been shown to be socioeconomically catastrophic especially to the rural poor, through a reduction in acquisition of human and physical capital (K. Asenso-Okyere & Asante, 2003; W. K. Asenso-Okyere & Dzator, 1997).

One of the critical goals of the AMFm design was to reach and impact rural areas, where the poorest of the poor, who also suffer disproportionately from malaria are found (Joel G Breman, Alilio, & Mills, 2004; Holtz et al., 2002; J. Sachs & Malaney, 2002;

Worrall et al., 2005). Inequities in access to health services, including to antimalarials, between the poor in rural areas and people of higher socio-economic status in urban areas have consistently been noted (Cohen et al., 2010; MMV, 2008). Also, there is evidence that both retail outlet characteristics and practices of retailers differ across rural and urban areas (Wafula et al., 2012). Thus, one measure of the success of the AMFm was whether the intervention led to an increase in the use of ACTs, including among the poor in rural communities (Yamey et al., 2012).

Since antimalarials are available over-the-counter, consumers might be expected to exercise personal agency in requesting their preferred antimalarial during an encounter with a private retailer. Therefore one may be inclined to argue that while knowledge of the AMFm intervention and RRP among retailers is necessary, as shown by our study, of greater importance would be knowledge of the AMFm intervention by consumers. While this argument is plausible, findings from exit interviews from the logo study component of the IE suggest otherwise. Even though 61% of consumers said they had seen the AMFm logo before, 85% purchased a particular antimalarial based on recommendations from the retailer, friends, or family. No consumer purchased a particular treatment because they heard of the drug from radio/TV, and only 2.3% purchased a particular antimalarial because they thought it was inexpensive (AMFm IE Team, 2012). This suggests that the consumer knowledge of the AMFm and arguably even about the RRP, might not necessarily determine their choice of drug. Consumers did not exercise personal agency, but rather deferred choice to the retailer. This finding of choice of antimalarial treatment being determined by the retailer brings into question the extent to

which a patient-centered approach is being pursued in the Ghanaian private health service delivery sector (Ghana News Agency, 2013).

Our data showed that 93.4% of private-sector retailers (97.3% in the urban and 87.3% in rural areas) recognized the green-leaf logo. Of those retailers who had seen or heard of the logo, 78.3% stated that their source was radio/TV (83.7% in the urban and 69% in the rural areas). This suggests that among retailers in Ghana, radio/TV is a critical source of knowledge. Our findings reinforce the hypothesis that the retailer's, as opposed to the consumers' knowledge, was most critical to the outcomes of the AMFm. The pilot study carried out in Tanzania to provide insight into whether AMFm medicines had the potential to reach poor rural communities, also showed that the recommendation of a provider was an important factor in the consumer's decision to purchase an ACT (Cohen et al., 2010).

Our analyses further reveals that while there was no disparity between rural and urban outlets in exposure to training (unadjusted OR=1.19, $p=0.56$), the positive effect of training on knowledge of the RRP was significantly weaker in urban areas than in rural areas (adjusted OR of the interaction=0.15, $p=0.001$). In fact, in urban areas, training did not have any significant effect (the marginal effect, $p=0.208$). We believe that this difference is due to there being many other sources of knowledge of the AMFm beyond training, especially in urban areas, allowing less room for improvement in knowledge with training in urban areas compared to rural areas. These other sources of knowledge include over 10,000 radio spots and 400 television commercials on the AMFm aired in

English and 7 other local languages across the country between the baseline and endline survey periods (AMFm IE Team, 2012).

Inequities in ownership of radio and TV, and by extension electricity and other amenities in general, are likely to be associated with inequities in knowledge of the AMFm program and the RRP between urban and rural outlets, particularly in the private sector. Overcoming these inequities requires extra effort to be made in carrying out Information Education & Communication (IE&C) and Behavior Change Communication (BCC) training activities in rural areas, in order to achieve outcomes equitable to those in urban areas. We suggest that the inequity in knowledge of the AMFm and the RRP between urban and rural areas seen from our analyses could be attributable in part to an unintentional failure to recognize urban/rural differences and to adapt supporting interventions sufficiently enough to address these by focusing more on rural areas.

Intuitively, it makes sense that greater IE&C, BCC, training and other efforts to disseminate knowledge be focused on rural areas, which often tend to be areas of high malaria prevalence. The AMFm stakeholders were particularly concerned that rural residents would be disadvantaged over urban residents regarding access to the co-paid QAACs. Those in the lower wealth quintiles who stand to benefit the most from co-paid QAACs live in rural areas, which often have the highest malaria prevalence in the country. We acknowledge that there often tends to be an association between rural-ness and high malaria prevalence. Nevertheless we argue that simply focusing more knowledge-generating activities in rural and high malaria prevalence areas might not necessarily lead to improved AMFm outcomes such as increased stocking of co-paid

QAACTs, their use, and a resulting decrease in morbidity/mortality from malaria. We make this argument because the high number of cases-per-outlet seen in the high prevalence areas and northern savanna zones suggests that there are simply not enough outlets to serve the cases (see Tables 16a and 16b). Thus, even achieving complete coverage and saturation in AMFm knowledge among retailers might not mitigate the problem of access to outlets and co-paid QAACTs.

An integrated systems approach (Gyapong et al., 2010) is therefore needed to ensure optimal outcomes of interventions involving drug subsidies such as the AMFm (Atun, de Jongh, Secci, Ohiri, & Adeyi, 2010; Cavalli et al., 2010; de Savigny & Adam, 2009). We therefore recommend that in addition to increasing the proportion of retailers trained and intensifying other SIVs in high prevalence and rural areas, ongoing measures aimed directly at increasing access to outlets and driving down the case-outlet ratio are intensified. These measures include building of Community-based Health Planning and Services compounds (GoG, 2013; Nyonator, Awoonor-Williams, Phillips, Jones, & Miller, 2005), promoting the use of long lasting insecticide treated nets, and carrying out indoor residual spraying (Yakob, Dunning, & Yan, 2011).

The AMFm IE in Ghana investigated the percentage of the population living in clusters with at least one outlet that stocked QAACTs. Even before the AMFm (at baseline), the IE report showed that Ghana already had 100% coverage for this measure (see Appendix 25). However in interpreting this indicator, it should be noted that the study design aimed to choose sample clusters with a population size of about 10,000-15,000. In Ghana, the population size per cluster was often much larger, and these

clusters did not represent any formal administrative area. This means that having at least one QAACT-stocking outlet available in the cluster did not necessarily reflect reasonable access for the whole population. Also, this measure does not reflect other dimensions of access such as information, retailer behavior and affordability (AMFm IE Team, 2012; J. Amuasi et al., 2012).

There are a number of limitations to our study. While we adjusted for differences in malaria prevalence between urban and rural areas, we did not account for differences in exposure to sources of knowledge other than AMFm training, such as radio and TV advertisements. Access to these other sources of knowledge is influenced by various socio-economic factors which also tend to differ between rural and urban areas. We were unable to take these other sources of knowledge into account, although it is fair to say these unmeasured factors are often correlated with malaria prevalence (J. Sachs & Malaney, 2002; Worrall et al., 2005). Since we controlled for malaria prevalence, these unmeasured factors are unlikely to have changed our conclusions.

More important however, are the definitions of urban and rural. In Ghana and most of sub-Saharan Africa, definitions of urban or rural are used for census area classifications, survey sampling, and evaluation of geographic and socio-economic equity. However, restricting the definition of a location to the binary of urban or rural has often been viewed as too simplistic to properly describe the significant variations in a population's potential access to services (Harpham & Tanner, 1995) [page 36] (Wang, 2005). In Ghana for example, there are also some rural areas in the coastal zone that may have better access to knowledge than urban areas in the northern savanna zone. Thus

population density and resources are not completely correlated. In the USA, these concerns about rural/urban classification led to the creation of Rural-Urban Commuting Area Codes to better aid research and inform policy (Hart, Larson, & Lishner, 2005).

By creating indices such as population per outlet and cases per outlet (see Tables 16a and 16b), we invariably suggest that there is homogeneity in access within malaria prevalence or ecologic zones. However it is reasonable to believe that the number of cases per outlet would vary widely within malaria prevalence or ecologic zone as a result of many factors such as outlet type and size. Nevertheless at the aggregated level, this should not compromise the overall policy implications of our findings.

Our study shows the importance of training as part of the AMFm in generating knowledge of the RRP for co-paid QAACTs among retailers, particularly in rural areas. We also see that because avenues for acquiring knowledge are limited in rural areas, dwellers end up being further disadvantaged when no significant extra effort is put into making knowledge of the intervention available directly to the population. Particularly in rural areas with high malaria prevalence, improving access to knowledge among retailers must be combined with improving access to services among consumers, and intensifying efforts at lowering prevalence.

Table 14: Unweighted distribution of sample characteristics

Characteristics		Private for-profit outlets
<i>Total: N, %</i>		648, 100%*
Respondent knew and specified the RRP for co-paid QAACTs		81.9
At least 1 employee from the outlet received training on QAACTs with the logo		46
Malaria testing (microscopy/RDT) available at the outlet		4.5
At least 1 employee completed secondary school		92.3
At least 1 employee is a pharmacist, nurse or doctor		51.4
Type of outlet	<i>Licensed chemical shop</i>	53.7
	<i>Pharmacy</i>	41.8
Location	<i>Urban</i>	73.2
	<i>Rural</i>	26.9
Number of employees	<i>One</i>	13.7
	<i>Two</i>	36.4
	<i>Three</i>	22.1
	<i>Four or more</i>	26.5
Malaria epidemiologic zone**	<i>Coastal savanna/Mangrove swamps</i>	47.8
	<i>Tropical rain forest</i>	38.1
	<i>Northern savanna</i>	14
<i>Falciparum</i> malaria prevalence (%)	<i>Low (10-24)</i>	33.3
	<i>Medium (25-34)</i>	32.3
	<i>High (35-70)</i>	34.4

*Percentages may not add up to 100% because of rounding or missing data

§ Approximation based on demarcations of ecological zones (Coastal, Forest and Northern) used by the Ghana Statistical Service

RRP: Recommended Retail Price

QAACCT: Quality Assured Artemisinin-based Combination Therapy

Table 15: Adjusted odds ratio of knowing the RRP for various outlet characteristics

Outlet Characteristics		Knowledge of the RRP	
		Odds Ratio	p-value
Location and Training categories (using rural and untrained as the reference group)***	Rural and Untrained	Ref.	-
	Rural and Trained	10.23	* <0.001
	Urban and Untrained	9.53	* <0.001
	Urban and Trained	14.60	* <0.001
Location and Training categories (using urban and untrained as the reference group)***	Rural and Untrained	0.10	* <0.001
	Rural and Trained	1.07	0.854
	Urban and Untrained	Ref.	-
	Urban and Trained	1.53	0.204
Trained vs. Untrained [§]	Rural	Ref.	*0.001
	Urban	0.15	
Type of outlet	Licensed chemical shop	Ref.	0.162
	Pharmacy	1.81	
At least 1 employee completed secondary school	No	Ref.	0.187
	Yes	2.04	
Malaria testing available	No	Ref.	0.937
	Yes	1.05	
At least 1 employee is a pharmacist, nurse or doctor	No	Ref.	0.719
	Yes	0.90	
Number of employees	One	Ref.	0.273
	Two	0.68	
	Three	0.75	
	Four or more	1.38	
Malaria epidemiologic zone**	Coastal savanna/Mangrove swamps	Ref.	0.885
	Tropical rain forest	1.25	
	Northern savanna	1.09	
<i>Falciparum</i> malaria prevalence (%)	Low (10-24)	Ref.	0.342
	Medium (25-34)	0.44	
	High (35-70)	0.44	

P-values were derived from χ^2 tests of significance of the differences in adjusted survey weighted odds ratios of the outcomes for each variable

**Statistically significant p-value (≤ 0.05)*

***Approximation based on demarcations of ecological zones (Coastal, Forest and Savanna) used by the Ghana Statistical Service*

****Training refers to an employee from the outlet receiving training on QAACs with the logo. Location is either urban or rural*

*§This is the interaction (location*training) and the OR is really a ratio of ratios*

QAAC: Quality Assured Artemisinin-based Combination Therapy

RRP: Recommended Retail Price

Table 16a: Malaria epidemiologic zone, population, and number of cases per annum for public and private sector outlets within censused clusters[†]

Population/Cases	Malaria Epidemiologic Zones*, N=512		
	Coastal (n=194)	Forest (n=216)	Savanna (n=102)
	<i>Actual</i>	<i>Actual</i>	<i>Actual</i>
Population exposed	245,472	349,662	206,236
Number of cases**	69,280	133,303	116,842
Number of cases (standardized to coastal zone)	-	93,582	139,071
Population per outlet (public and private)	1,265	1,619	2,022
Cases per outlet (public and private)	357	617	1,146

[†]"Censused clusters" refers to clusters within which all outlets with the potential to sell antimalarials were visited

*Approximation based on demarcations of ecological zones (Coastal, Forest and Savanna) used by the Ghana Statistical Service

**Number of cases=Prevalence*population

Table 16b: Malaria prevalence, population, and number of cases per annum for public and private sector outlets within censused clusters[†]

Population/Cases	Malaria Prevalence (%), N=512		
	Low, 10-24 (n=122)	Mid, 25-34 (n=151)	High, 35-70 (n=239)
	<i>Actual</i>	<i>Actual</i>	<i>Actual</i>
Population exposed	95,854	251,219	454,297
Number of cases**	15,378	76,175	227,872
Number of cases (standardized to low prevalence area)	-	29,065	48,080
Population per outlet (public and private)	786	1,664	1,141
Cases per outlet (public and private)	126	504	573
[†] "Censused clusters" refers to clusters within which all outlets with the potential to sell antimalarials were visited			
*Approximation based on demarcations of ecological zones (Coastal, Forest and Savanna) used by the Ghana Statistical Service			
**Number of cases=Prevalence*population			

Chapter 6: Conclusions and Future Implications

This 3-paper dissertation examined the relationship between training on the Affordable Medicines Facility – malaria (AMFm) co-paid quality assured artemisinin-based combination therapies (QAACTs), knowledge of the AMFm and the recommended retail price (RRP) for QAACTs, and stocking of QAACTs.

Accounting for 33.7% of all deaths in children under-five years, malaria is a disease of great public health importance in Ghana, and the entire Ghanaian population of 25 million lives at risk of the disease. The World Health Organization (WHO) specifically recommends artemisinin-based combination therapies (ACTs) as first-line treatment for uncomplicated *P. falciparum* malaria. In this regard, the Ghana National Malarial Control Program (NMCP) has included in its national strategic plan for malaria, to by 2015, be treating 90% of malaria patients with ACTs.

However low uptake of ACTs persists, largely been on account of the following:

1) ACTs are provided almost entirely by the public sector, and over 60% of patients access anti-malarial treatment through the private sector, 2) in the private sector ACTs are hardly available because they are much more expensive than other non-recommended antimalarials and so many patients, particularly in rural areas, are unable to afford them, 3) overall there are fewer outlets for obtaining ACTs in rural areas than in urban areas, even though the burden of malaria is higher in rural areas.

Therefore the AMFm was introduced as a factory-gate negotiation and co-payment (made by the Global Fund) of up to 95% of the QAACTs, along with a number of supporting interventions. These QAACTs were identified by a green leaf logo and had

a RRP equivalent to USD 0.96. Having been made affordable to consumers in both the public and private health sectors, the co-paid QAACTs were expected to become the antimalarial of choice for even the most rural and poor populations. The AMFm was run as a 2-year pilot in 7 countries including Ghana, starting in 2010.

The Global Fund commissioned an Independent Evaluation (IE) of the AMFm in each pilot country to assess the achievement of the AMFm objectives by measuring changes between baseline and endline surveys in availability, price, market share and use of QAACTs. The AMFm IE in Ghana showed that particularly in the private sector, the promotion of the AMFm led to a high provider awareness of the intervention, its logo, and RRP at endline. Correspondingly, QAACT availability across all outlets in Ghana increased by 52 percentage points, from 31% at baseline to 83% at endline ($p < 0.0001$).

Using data from the AMFm IE endline survey, this research contributes to the emerging body of knowledge on the outcomes of the AMFm in Ghana by exploring “*why*” and “*how*” the outcomes documented in the IE report came to be observed, specifically by: 1) exploring the relationship between various outlet characteristics and QAACT stocking in both the public and private sector; 2) further examining QAACT pricing by determining factors accounting for outlet’s adherence to their recommended retail price in the private-for-profit sector; and 3) identifying differences between urban and rural outlets in the impact of training on knowledge of the recommended retail price for co-paid QAACTs in private-for-profit outlets.

Predictors of Stocking QAACTs

Chapter 3 of this dissertation was based on the premise that public and private sector outlets function differently, and we examined outlet characteristics and how they are able to predict outlets that did and those that did not have QAACTs in stock.

We found that factors associated with QAACT stocking varied between and public and private sectors for the three QAACT availability definitions we created: i) Stocked some QAACTs, ii) Stocked some co-paid QAACT, and iii) Stocked some co-paid QAACTs without stocking any oral artemisinin monotherapies or non-artemisinin therapies. While a high percentage of public and private outlets stocked at least one co-paid QAACT, public sector outlets were by far better at stocking QAACTs than private sector outlets when not stocking artesunate monotherapies (AMTs) and non-artemisinin therapies (nATs) was included in the definition of QAACT stocking.

In the private sector, having received training was associated with a high predicted probability of stocking some QAACTs and stocking at least one co-paid QAACT, but not with stocking some co-paid QAACTs without stocking any oral AMTs or nATs. However in the public sector, training was not a statistically significant predictor of any definition of QAACT availability.

We concluded that in-service training is generally an important tool towards improving QAACT stocking practices especially in the private sector, where stocking decisions are often made by the outlet owner or manager in consultation with prescribers/dispensers and based on consumer demand, reflected by sales figures. However, the larger more complicated nature of the private sector antimalarial market

makes it more difficult to be regulated, monitored and aligned with national policy, where QAACTs are to be stocked and oral AMTs and nATs not stocked. Therefore beyond training, we recommend that approaches to improving policy adherence in the private sector, such as imposing severe penalties on importers of oral AMTs and nATs, coupled with explicit campaigns vilifying their use should be adopted by policy makers. In the public sector, stocking decisions and the organization of service delivery mechanisms are made centrally (at district and regional level). Thus, as expected, training was not a significant predictor of any of our stocking outcomes.

For both public and private sector outlets however, our findings suggested that efforts at improving QAACT stocking need to pay special attention to smaller outlets, especially those with 1-2 employees. We further recommended that getting outlets to hire staff with health-related qualifications should be pursued as an effective long-term approach towards achieving ACT stocking benchmarks and recommended treatment practice.

Adherence to the Recommended Retail Price

Chapter 4 further examined QAACT pricing by determining factors accounting for outlet's adherence to the recommended retail price in the private-for-profit sector. This study addresses stakeholder's concerns that retailers, who are the final interface between the patient and the QAACT, could seize the opportunity to make super-normal profits and not pass the high-level AMFm subsidy on to consumers.

Our study indicated that although retailer's adherence to the RRP for co-paid QAACTs can be high when knowledge about the RRP is present, knowledge was

associated with a much higher predicted probability of stocking some co-paid QAACTs at RRP than stocking all at RRP. We also presented convincing evidence that aside from knowledge, there are other important factors to consider if improvement in adherence to the RRP is desired.

We also found that in stocking co-paid QAACTs, stocking AL only led to a higher predicted probability of stocking some or all at RRP than stocking ASAQ only, and a higher predicted probability of stocking all at RRP than stocking both ASAQ and AL. A bias in stocking in favor of adult formulations for AL and pediatric formulations for ASAQ was also found, and we concluded that these phenomena are likely to be a reflection of existing consumer preferences, which have been observed and echoed by the National Malaria Control Program.

Our study led us to recommend that information on the AMFm subsidy be disseminated with greater focus on areas of high malaria prevalence, such as the northern savanna zone. Innovative ways of delivering information on the subsidy tailored specifically to these high Pfpr areas is more likely to increase awareness of the availability and RRP of the co-paid QAACTs than more generalized approaches. We also recommended that the Ministry of Health in Ghana consider adopting a policy supporting the use of ASAQ for children and AL for adults for the treatment uncomplicated malaria. Our findings and other sources indicate that this population segmentation approach to multiple first-line antimalarial therapy is already the *de-facto* situation in Ghana. Thus by taking advantage of a situation that has already been created naturally by market forces,

the message on co-paid QAACTs and their importance for treatment of uncomplicated malaria can be reinforced to allow for even better compliance with RRP.

Urban-rural Variations in the impact of training on knowledge

Finally, Chapter 5 identified and examined differences between urban and rural outlets in the impact of training on knowledge of the recommended retail price for co-paid QAACTs in private-for-profit outlets.

We found that that training raised outlets in rural locations to an odds ratio of having knowledge of the RRP equivalent to that of outlets in urban locations that had not undergone any training (rural untrained outlets as reference group). We therefore concluded that knowledge of the RRP as an outcome of having received training was particularly important for rural outlets. We believe that this difference in impact of training in favor of rural outlets is due to there being many other sources of knowledge of the AMFm beyond training. These “other sources” are more accessible in urban areas, and include radio and TV. Inequities in ownership of radio and TV, and by extension electricity and other amenities in general, are likely to be associated with inequities in knowledge of the AMFm program and the RRP between urban and rural outlets, particularly in the private sector. Overcoming these inequities requires extra effort to be made in carrying out Information Education & Communication (IE&C) and Behavior Change Communication (BCC) training activities in rural areas, in order to achieve outcomes equitable to those in urban areas.

Based on these findings and estimates of malaria cases per outlet across malaria epidemiologic zones in Ghana, we recommended that ongoing measures aimed directly at

increasing access to outlets and driving down the case-outlet ratio be intensified along with increasing the proportion of retailers trained and intensifying other supporting interventions in high prevalence and rural areas.

In countries like Ghana, where the AMFm pilot was shown to be highly successful, the government has expressed willingness to voluntarily commit some of their future Global Fund resource allocation and other resources to antimalarial drug subsidies post the AMFm. This dissertation therefore lends insight to some of what accounted for the findings of the AMFm IE in Ghana, informs policy in the proposed continuation of an antimalarial subsidy in the private sector, and is useful for the future design of further interventions involving subsidies for essential medicines.

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Appendices

Appendix A

Codebook for Appendices

Variable Code	Description
allqaactRRP	All co-paid QAACTs sold at or below RRP (yes/no)
allqaactRRP_oneUSD	All co-paid QAACTs sold at or below 1 USD (yes/no)
AP_QWLprivate	Formulation of co-paid QAACTs (1-adult only; 2-both adult and pediatric)
AtleastqaactRRP	At least 1 co-paid QAACTs sold at or below RRP (yes/no)
AtleastqaactRRP_oneUSD	At least 1 co-paid QAACTs sold at or below 1 USD (yes/no)
Cat3_healthqual	Category of highest health-related qualification (1-Non-health-related; 2-No formal training or certification for prescribing or dispensing medications; 3-Formally trained to prescribe or dispense medications)
Cat3_NoOfPrescribers	Number of prescribers/dispensers employed (1-1-2; 2-3-4; 3-5 or more)
Cat3_numberofqaactwithlogo	Number of co-paid QAACTs audited (1-1; 2-2-3; 3-4 or more)
Cat3_PPfpr	Falciparum malaria prevalence (%) (1-low; 2-mid; 3-high)
Cat4_NoOfWorkers_auto	Number of employees/workers (1-1; 2-2; 3-3; 4- 4 or more)
EcolZoneCFS	Malaria epidemiologic zone (1-Coastal; 2-Forest; 3-Savanna)
fixedoutAmCat4	Stocked at least 1 nAT (yes/no)
healthqualind	At least 1 employee is a pharmacist, nurse or doctor (yes/no)
identRrp	Respondent knew and specified the RRP (yes/no)
outAmCat1	Stocked at least 1 QAACT (yes/no)
outAmCat1_logo	Stocked at least 1 co-paid QAACT (yes/no)
outAmCat1_nologo	Stocked some non-AMFm QAACTs (yes/no)
outAmCat2	Stocked at least 1 non-QAACT (yes/no)

(Continued) Codebook for Appendices

Variable Code	Description
outAmCat3_Oral	Stocked at least 1 oral AMT (yes/no)
Owner	The respondent owned the outlet (yes/no)
pharmlcs	The outlet is either a pharmacy or a LCS (1-pharmacy; 2-LCS)
second	At least 1 employee had completed secondary school (yes/no)
test	Malaria testing (microscopy/RDT) available (yes/no)
trainedProg	At least 1 employee from the outlet received training on QAACts with the logo (yes/no)
typeQWLavail	Active ingredients of co-paid QAACts (1-ASAQ; 2-AL; 3-both ASAQ & AL)
Urban	Urban or rural outlet (1-urban; 2-rural)

Appendix B

Weighting

To account for these design features in the tabulations, the STATA commands for analyzing complex survey data (“svy” commands) were used to weight the data and calculate confidence intervals taking clustering and stratification into account.

The IE team declared the primary sampling unit (district), the weight variable (wt), the strata and the finite population correction (fpc) factor equaling the sampling fraction for each stratum (the number of sampled subdistricts in a stratum divided by the total number of subdistricts in the stratum, or 0.5 if the sampling fraction was greater than 50 percent).

Data were survey set as follows:

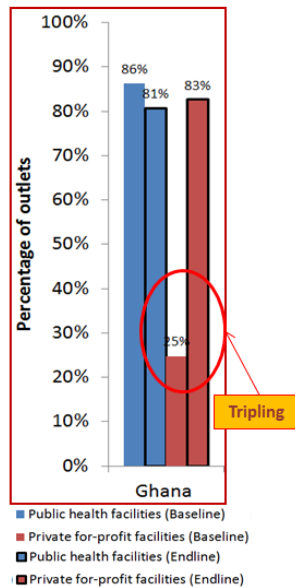
```
svyset district [pweight=wt ], strata(strata) fpc(fpc)
```

The team calculated a proportion and its 95 percent confidence interval (CI) as follows:

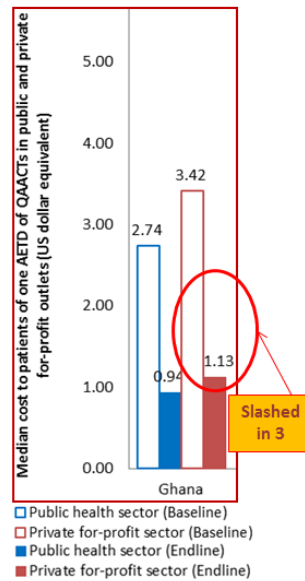
```
svy: proportion VariableName
```

Appendix 1

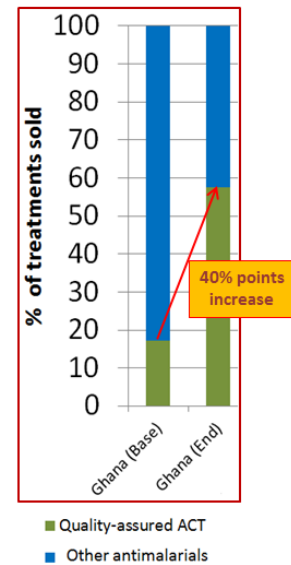
Summary of AMFm outcomes in Ghana



Stocking: Largest rise was in private for profit outlets, with an increase in QAACT availability of 58% points. No change in public (86% at baseline)



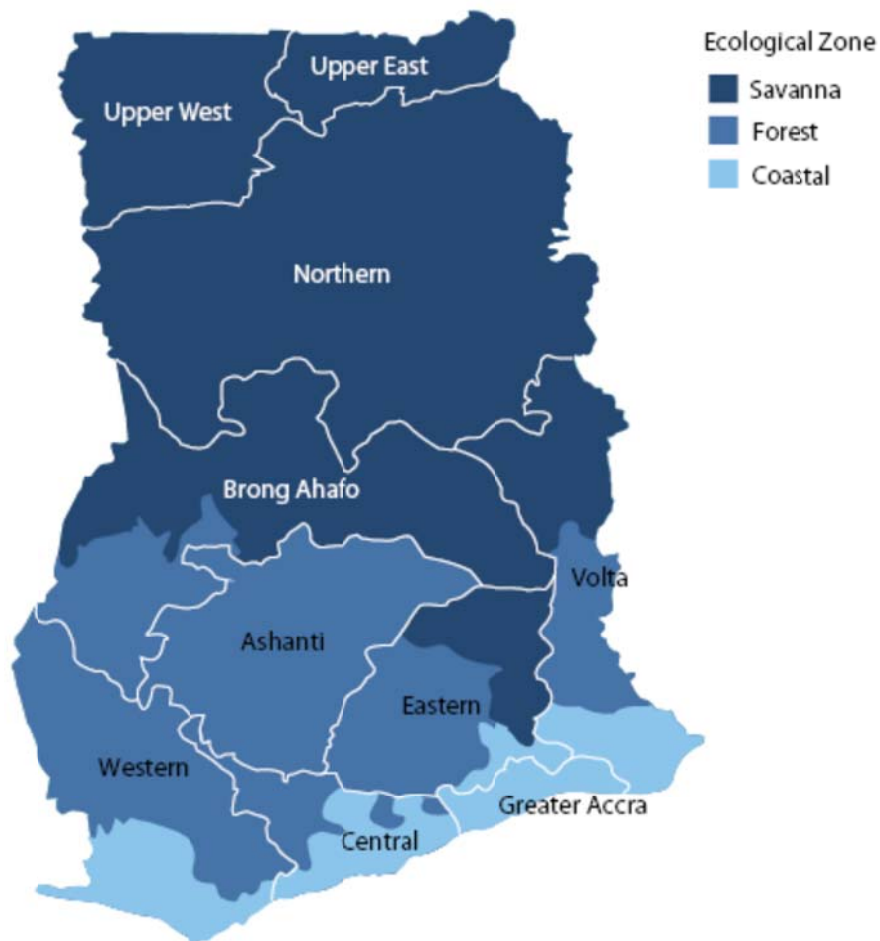
Price: Fell from USD 2.74 to USD 0.94 in public sector. In private for-profit sector, fell from USD 3.42 to USD 1.13 Slightly higher than the RRP of USD 0.96



Market share: Overall, increased by 40% points; from baseline to endline of all antimalarials sold/ distributed

Appendix 2

Map of Ecological Zones and Regions, Ghana 2011



Source: GSS. (2011). Ghana Multiple Indicator Cluster Survey with an Enhanced Malaria Module and Biomarker (Final). Accra, Ghana: Ghana Statistical Service. Retrieved from http://www.childinfo.org/files/Ghana_2011_MICS_Final_Report.pdf

Appendix 3

Output from the private sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 QA ACT”, excluding the variable “Malaria testing (microscopy/RDT) available”, because it was not significant in the unadjusted analysis

outAmCat1	Odds Ratio	Linearized Std. Err.	t	P> t	[95% Conf. Interval]	
1.trainedProg	1.896891	.5367442	2.26	0.028	1.075102	3.346841
1.second	1.208237	.3790141	0.60	0.549	.6438391	2.267394
Cat3_healthqual						
1	1.221203	.4613034	0.53	0.599	.5722583	2.606054
2	4.359817	1.84429	3.48	0.001	1.865592	10.18873
Cat3_NoOfPrescribers						
2	1.279675	.406632	0.78	0.441	.6763601	2.421149
1.Urban	1.145032	.3051363	0.51	0.613	.670781	1.954586
EcolZoneCFS						
2	.8701382	.3425126	-0.35	0.725	.3949564	1.917023
3	.6159108	.2539013	-1.18	0.245	.2693167	1.40855
_cons	1.869555	.7369135	1.59	0.118	.8476821	4.123288

	df	F	P>F
Cat3_healthqual	2	10.65	0.0001
Design	52		

	df	F	P>F
EcolZoneCFS	2	0.99	0.3779
Design	52		

From this model excluding the variable “Malaria testing (microscopy/RDT) available”, the p-value for training is even lower than in the model selected (0.028 vs. 0.039). However we selected the model in the manuscript in order to maintain homogeneity in the model for the 3 different outcomes. The model in the manuscript was selected also because the general interpretation of the results did not change with the exclusion of the variable “Malaria testing (microscopy/RDT) available”.

Appendix 4

Output from the private sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 co-paid QAAC”, excluding the variable “Malaria testing (microscopy/RDT) available”, because it was not significant in the unadjusted analysis

outAmCat1_logo	Odds Ratio	Linearized Std. Err.	t	P> t	[95% Conf. Interval]	
1.trainedProg	1.93456	.5055809	2.52	0.015	1.145063	3.268398
1.second	1.319177	.424247	0.86	0.393	.6918893	2.515182
Cat3_healthqual						
1	1.269758	.4772431	0.64	0.528	.597274	2.699406
2	3.574426	1.349838	3.37	0.001	1.675345	7.626203
Cat3_NoOfPrescribers						
2	1.079444	.3019245	0.27	0.786	.6158077	1.892148
3	3.15204	2.173213	1.67	0.102	.7902091	12.57307
1.Urban	1.20814	.3177029	0.72	0.475	.712765	2.047802
EcolZoneCFS						
2	.9818793	.3588588	-0.05	0.960	.4715739	2.044402
3	.6750887	.2571717	-1.03	0.307	.3143232	1.449924
_cons	1.486041	.5709749	1.03	0.307	.687365	3.212728

	df	F	P>F
Cat3_healthqual	2	10.36	0.0002
Design	52		

	df	F	P>F
Cat3_NoOfPrescribers	2	1.62	0.2082
Design	52		

	df	F	P>F
EcolZoneCFS	2	1.05	0.3570
Design	52		

From this model excluding the variable “Malaria testing (microscopy/RDT) available”, the p-value for training is even lower than in the model selected (0.015 vs. 0.020). However we selected the model in the manuscript in order to maintain homogeneity in the model for the 3 different outcomes. The model in the manuscript was selected also

because the general interpretation of the results did not change with the exclusion of the variable “Malaria testing (microscopy/RDT) available”.

Appendix 5

Output from the private sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 QAACT”, substituting the variable “Category of highest health-related qualification” (Cat3_healthqual) with “At least 1 employee is a pharmacist, nurse or doctor” (healthqualind)

outAmCat1	Odds Ratio	Linearized Std. Err.	t	P> t	[95% Conf. Interval]	
1.trainedProg	1.934865	.5610293	2.28	0.027	1.081333	3.462118
1.test	.6669057	.3898409	-0.69	0.491	.2063677	2.155197
1.second	1.619007	.460905	1.69	0.097	.914437	2.866446
1.healthqualind	4.12042	1.348712	4.33	0.000	2.13642	7.946875
Cat3_NoOfPrescribers						
2	1.335207	.4178673	0.92	0.360	.7125433	2.501994
3	1	(empty)				
1.Urban	1.212351	.3192922	0.73	0.468	.7146793	2.05658
EcolZoneCFS						
2	.8505311	.3264063	-0.42	0.675	.3937731	1.837107
3	.5367116	.2000733	-1.67	0.101	.2540245	1.133982
_cons	1.502512	.5865469	1.04	0.302	.6864575	3.288686
	df	F	P>F			
EcolZoneCFS	2	1.76	0.1830			
Design	52					

Following the variable substitution, the p-value for training is lower than in the model selected (0.027 vs. 0.039). However the general interpretation of the results does not change.

Appendix 6

Output from the private sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 QAACT”, substituting the variable “Number of prescribers/dispensers employed” (Cat3_NoOfPrescribers) with “Number of employees” (Cat4_NoOfWorkers_auto)

outAmCat1	Odds Ratio	Linearized Std. Err.	t	P> t	[95% Conf. Interval]	
1.trainedProg	1.873454	.5219018	2.25	0.028	1.071198	3.276547
1.test	.6787382	.4032137	-0.65	0.517	.2060584	2.235704
1.second	1.320129	.4428995	0.83	0.412	.6733464	2.588177
Cat3_healthqual						
1	1.208561	.4831158	0.47	0.638	.5418772	2.695481
2	5.596556	3.160236	3.05	0.004	1.802272	17.37887
Cat4_NoOfWorkers_auto						
1	.8528383	.2570929	-0.53	0.600	.4657529	1.561629
2	.7143285	.279591	-0.86	0.394	.3256859	1.56674
3	.7697251	.4809602	-0.42	0.677	.2196833	2.696959
1.Urban	1.138053	.2935647	0.50	0.618	.6782074	1.909689
EcolZoneCFS						
2	.8321154	.2990669	-0.51	0.611	.4045483	1.711578
3	.5758858	.2368292	-1.34	0.185	.2523177	1.314392
_cons	2.229629	.83272	2.15	0.036	1.053791	4.717486

	df	F	P>F
Cat3_healthqual	2	9.59	0.0003
Design	52		

	df	F	P>F
Cat4_NoOfWorkers_auto	3	0.25	0.8623
Design	52		

	df	F	P>F
EcolZoneCFS	2	1.09	0.3454
Design	52		

Following the variable substitution, the p-value for training is lower than in the model selected (0.028 vs. 0.039). However the general interpretation of the results does not change.

Appendix 7

Output from the private sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 QAACT”, substituting variables “Category of highest health-related qualification” (Cat3_healthqual) and “Number of prescribers/dispensers employed” (Cat3_NoOfPrescribers) with “At least 1 employee is a pharmacist, nurse or doctor” (healthqualind) and “Number of employees” (Cat4_NoOfWorkers_auto) respectively

outAmCat1	Odds Ratio	Linearized Std. Err.	t	P> t	[95% Conf. Interval]	
1.trainedProg	1.976544	.5619661	2.40	0.020	1.117199	3.496892
1.test	.7091621	.4278079	-0.57	0.571	.2113589	2.379416
1.second	1.73856	.540635	1.78	0.081	.9315142	3.244815
1.healthqualind	5.117675	2.306947	3.62	0.001	2.071231	12.64494
Cat4_NoOfWorkers_auto						
1	.8753062	.2521267	-0.46	0.646	.4910624	1.560211
2	.7619214	.2810496	-0.74	0.464	.363454	1.597243
3	.7813623	.4989506	-0.39	0.701	.2169495	2.814144
1.Urban	1.207329	.3025959	0.75	0.456	.7301394	1.996392
EcolZoneCFS						
2	.8198255	.2870824	-0.57	0.573	.4060246	1.655352
3	.5182838	.1922047	-1.77	0.082	.2462535	1.09082
_cons	1.70397	.6325797	1.44	0.157	.8089771	3.589116

	df	F	P>F
Cat4_NoOfWorkers_auto	3	0.18	0.9117
Design	52		

	df	F	P>F
EcolZoneCFS	2	1.82	0.1726
Design	52		

Following the variable substitution, the p-value for training is lower than in the model selected (0.020 vs. 0.039). However the general interpretation of the results does not change.

Appendix 8

Output from the public sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 QA ACT”, excluding the variable “Category of highest health-related qualification” (Cat3_healthqual)

outAmCat1	Odds Ratio	Linearized Std. Err.	t	P> t	[95% Conf. Interval]	
1.trainedProg	.9773964	.3103179	-0.07	0.943	.516871	1.848244
Cat3_NoOfPrescribers						
2	2.426027	.6114205	3.52	0.001	1.463059	4.022812
3	3.161391	1.537797	2.37	0.022	1.191148	8.390552
1.Urban	.651126	.2824855	-0.99	0.327	.2726357	1.555061
EcolZoneCFS						
2	.7018858	.3524644	-0.70	0.484	.2562356	1.92262
3	2.656754	1.589971	1.63	0.109	.7994748	8.828726
_cons	2.726727	1.538461	1.78	0.081	.8789051	8.459436

	df	F	P>F
Cat3_NoOfPrescribers	2	7.58	0.0013
Design	52		

	df	F	P>F
EcolZoneCFS	2	3.62	0.0338
Design	52		

In this model we exclude the variable “Category of highest health-related qualification” (Cat3_healthqual) based on the argument that in the public sector, since policy is fixed and all facilities are supposed to be manned by trained professionals, this variable would be unimportant. Following the variable exclusion, the general interpretation of the results does not change.

Appendix 9

Output from the public sector model showing the adjusted predictive power of training (trainedProg) for the outcome “stocked at least 1 QA ACT”, excluding the variable “Category of highest health-related qualification” (Cat3_healthqual) and substituting the variable “Number of prescribers/dispensers employed” (Cat3_NoOfPrescribers) with “Number of employees” (Cat4_NoOfWorkers_auto)

outAmCat1	Odds Ratio	Linearized Std. Err.	t	P> t	[95% Conf. Interval]	
1.trainedProg	1.07773	.3438558	0.23	0.815	.5681469	2.044368
Cat4_NoOfWorkers_auto						
1	1.474161	.8657724	0.66	0.512	.4536582	4.790283
2	1.343505	.6238488	0.64	0.528	.5291445	3.411175
3	1.487179	.5202753	1.13	0.262	.7370308	3.000825
1.Urban	.6297032	.2920018	-1.00	0.323	.2483254	1.596801
EcolZoneCFS						
2	.7389265	.3363269	-0.66	0.509	.2964448	1.841869
3	2.510021	1.455519	1.59	0.119	.7840133	8.035841
_cons	2.832003	1.469987	2.01	0.050	.999409	8.024983

	df	F	P>F
Cat4_NoOfWorkers_auto	3	0.42	0.7424
Design	52		

	df	F	P>F
EcolZoneCFS	2	2.71	0.0761
Design	52		

In this model we exclude the variable “Category of highest health-related qualification” (Cat3_healthqual) based on the argument that in the public sector, since policy is fixed and all facilities are supposed to be manned by trained professionals, this variable would be unimportant. We also replace the variable “Number of prescribers/dispensers employed” (Cat3_NoOfPrescribers) with “Number of employees” (Cat4_NoOfWorkers_auto) because they are both proxies for outlet size, and since prescribers are a sub-set of workers, the two cannot be used concurrently in a model. Following the variable exclusion and substitution, the non-significant role of training remains the same, while the number of turns out to be a non-significant predictor of the

outcome ($p=0.7424$). The variable “ecological zone” becomes border-line non-significant (p value was 0.029 in our selected model, but in this model it is 0.076).

Appendix 10

Discussion on the choice of proxies for outlet size

The number of workers, number of prescribers, number of antimalarials audited, number of antimalarial treatments sold in past week, and relative sales volume of QAACTs with logo sold are all measures that can be used as proxies to describe outlet size. However we believe the most appropriate proxy measure for size is the number of workers. We justify our position as follows: The number of workers reflects all the work associated with the outlet. The larger the outlet, the more workers are required to run it. There could be a rather small number of prescribers working in an outlet even though it may be large, making number of prescribers a less sensitive proxy for outlet size. Also, the number, sales volume, relative sales volume etc. of antimalarials may not adequately reflect its true size because the data limits us to information on only antimalarials and no other drugs. Further, if indeed per our hypothesis, malaria prevalence influences stocking and sales, then number of antimalarials audited or sales volumes will not adequately reflect outlet size.

Arguably, a better approach is not to use number of workers, number of prescribers, number of antimalarials audited, number of antimalarial treatments sold in past week, and relative sales volume of QAACTs with logo sold as proxy measures for outlet size *per se*, but rather as important characteristics than stand on their own and are interpreted literally. This is useful because each of the variables could hold policy relevance, especially if they were statistically significant in the adjusted model. We therefore ended up using only number of workers as proxy for size, and included number of co-paid QAACTs audited as an independent variable in our analyses. Using number of QAACTs audited is better than sales volume because there could be a high sales volume of a particular QAACT and no variety in the number of QAACTs audited, and that would not necessarily increase the chance of at least one QAACT being stocked at RRP (one of our outcome measures), compared to if there were several different QAACTs audited, which would increase the chance of one being at RRP, even though sales volume might be low or high.

Using a composite measure (such a ratio of AETD sold to number of workers) could be statistically elegant, but is not very useful from a policy perspective although it. Another challenge with creating and using this composite measure is that the AETDs of all antimalarials sold accounts for only antimalarials, and not all the drugs in the shop and so might bias the measure created.

See the following for examples of proxy measures for outlet size which support our choices:

1. Page 22 of: AHRQ. (2012). 2012 Preliminary Comparative Results: Pharmacy Survey on Patient Safety Culture (No. 12 - 0085 - 1 - EF) (p. 34). Rockville, MD: Agency for Healthcare Research and Quality. Retrieved from http://www.ahrq.gov/professionals/quality-patient-safety/patientsafetyculture/pharmacy/2012/PharmSOPS_PilotResults.pdf
2. Page 7 of: Heinsohn, J. G., & Flessa, S. (2013). Competition in the German pharmacy market: an empirical analysis. BMC Health Services Research, 13(1), 407. doi:10.1186/1472-6963-13-407

Appendix 11

Output from the model showing the adjusted predictive power of “Respondent knew and specified the RRP” (identRrp) for the outcome “At least 1 co-paid QAACTs sold at RRP” (AtleastqaactRRP) with inclusion of the variable “Stocked at least 1 non-QAACT” (outAmCat2)

AtleastqaactRRP	Odds Ratio	Linearized Std. Err.	t	P> t	[95% Conf. Interval]	
1.identRrp	10.29776	3.349853	7.17	0.000	5.361081	19.78031
Cat3_PPfpr						
1	1.545896	.2988966	2.25	0.029	1.048774	2.278656
2	1.972155	.5275619	2.54	0.014	1.152966	3.373381
typeQWLavail						
2	3.227687	1.258369	3.01	0.004	1.476154	7.057503
3	3.177604	1.284617	2.86	0.006	1.411842	7.151765
Cat3_numberofqaactwithlogo						
1	1.147761	.279015	0.57	0.573	.7046936	1.869403
2	2.133818	.7441649	2.17	0.034	1.05982	4.296183
1.outAmCat2	1.228805	.3002596	0.84	0.403	.7525526	2.006452
_cons	.0799426	.0375858	-5.37	0.000	.0311204	.2053576

	df	F	P>F
Cat3_PPfpr	2	5.48	0.0070
Design	52		

	df	F	P>F
typeQWLavail	2	4.68	0.0136
Design	52		

	df	F	P>F
Cat3_numberofqaactwithlogo	2	2.69	0.0774
Design	52		

In this model we include the variable “Stocked some non-QAACTs” (outAmCat2) because although it was significant in the unadjusted analysis ($p=0.040$), we did not include it in the adjusted model. It was excluded because we did not hypothesize any relationship between stocking particular classes of antimalarials and the outcome. Even if we find a statistical relationship between stocking non-QAACTs and stocking at least 1 co-paid QAACT at RRP, it is likely to be a function of outlet size, which we already

account for using the variable “Number of employees”. The included variable (Cat3_NoOfPrescribers) was non-significant in this adjusted analysis ($p=0.403$), and the general conclusions from our selected model do not change.

Appendix 12

Output from the model showing the adjusted predictive power of “Respondent knew and specified the RRP” (identRrp) for the outcome “All co-paid QAACTs sold at RRP” (allqaactRRP) with inclusion of the variables “Stocked some oral AMTs” (outAmCat3_Oral), “Stocked some non-AMFm QAACTs” (outAmCat1_nologo), “Stocked some non-QAACTs” (outAmCat2), and “Stocked at least 1 nAT” (fixedoutAmCat4)

	allqaactRRP	Odds Ratio	Linearized Std. Err.	t	P> t	[95% Conf. Interval]	
	1.identRrp	8.25939	3.819536	4.57	0.000	3.265398	20.89103
	1.Owner	1.400462	.3572607	1.32	0.193	.8393754	2.336612
	1.healthqualind	1.372549	.4127335	1.05	0.297	.7507064	2.509491
	1.urbrur	.7957971	.3032704	-0.60	0.552	.3704176	1.709673
	EcolZoneCFS						
	2	.9758725	.3448939	-0.07	0.945	.4801702	1.983312
	3	1.254869	.6156406	0.46	0.645	.4688684	3.358502
	Cat3_PPfpr						
	1	1.64426	.6345301	1.29	0.203	.7579883	3.566796
	2	1.641601	.6704967	1.21	0.230	.7233046	3.72575
	Cat4_NoOfWorkers_auto						
	1	.4841403	.1756909	-2.00	0.051	.2337326	1.00282
	2	.4914284	.2549549	-1.37	0.177	.1735143	1.391826
	3	.3547428	.2575651	-1.43	0.159	.0826359	1.522855
	typeQWLavail						
	2	3.264235	1.510069	2.56	0.014	1.290113	8.259146
	3	1.307988	.7332914	0.48	0.634	.4246513	4.028795
	1.AP_QWLprivate	.0514801	.026975	-5.66	0.000	.0179885	.1473274
	Cat3_numberofqaactwithlogo						
	1	.3241924	.107813	-3.39	0.001	.1663359	.6318582
	2	.0083454	.0077145	-5.18	0.000	.0013057	.0533388
	1.outAmCat3_Oral	.8867839	.2458497	-0.43	0.667	.5084077	1.546762
	1.outAmCat1_nologo	.887891	.2772713	-0.38	0.705	.4744763	1.661517
	1.outAmCat2	1.422769	.5703282	0.88	0.383	.6364975	3.180331
	1.fixedoutAmCat4	.9837043	.2397978	-0.07	0.947	.6031493	1.604369
	_cons	.1820575	.153868	-2.02	0.049	.0333942	.9925363
		df	F	P>F			
	EcolZoneCFS	2	0.14	0.8735			
	Design	52					

	df	F	P>F
Cat3_PPfpr	2	1.03	0.3637
Design	52		

	df	F	P>F
Cat4_NoOfWorkers_auto	3	1.33	0.2760
Design	52		

	df	F	P>F
typeQWLavail	2	5.95	0.0048
Design	52		

	df	F	P>F
Cat3_numberofqaactwithlogo	2	15.43	0.0000
Design	52		

In this model we include the four variables reflecting stocking various classes of antimalarials. We did not include these in the model we selected because although they were significant in the unadjusted analysis, we did not hypothesize any relationship between stocking particular classes of antimalarials and the outcome. Even if we find a statistical relationship between these added variables and stocking at least 1 co-paid QAACCT at RRP, it is likely to be a function of outlet size, which we already account for using the variable “Number of employees”. However, none of the included variables was significant in this adjusted analysis, and the general conclusions from our selected model do not change.

Appendix 13

Output from the model for the outcome “At least 1 co-paid QAACTs sold at <= 1 USD” (AtleastqaactRRP_oneUSD) instead of “At least 1 co-paid QAACTs sold at RRP” (AtleastqaactRRP)

AtleastqaactRRP_oneUSD	Odds Ratio	Linearized Std. Err.	t	P> t	[95% Conf. Interval]	
1.identRrp	10.53377	3.432102	7.23	0.000	5.478231	20.25476
Cat3_PPfpr						
1	1.471979	.2916105	1.95	0.056	.9891345	2.190522
2	1.90867	.5014428	2.46	0.017	1.126622	3.23358
typeQWLavail						
2	3.153474	1.21927	2.97	0.004	1.451573	6.850772
3	3.171005	1.279801	2.86	0.006	1.410828	7.127214
Cat3_numberofqaactwithlogo						
1	1.158661	.2799667	0.61	0.545	.7134806	1.881614
2	2.16562	.7729834	2.16	0.035	1.058091	4.432427
_cons	.0942585	.0416519	-5.34	0.000	.0388351	.2287795

	df	F	P>F
Cat3_PPfpr	2	4.75	0.0128
Design	52		

	df	F	P>F
typeQWLavail	2	4.61	0.0144
Design	52		

	df	F	P>F
Cat3_numberofqaactwithlogo	2	2.62	0.0827
Design	52		

There is no change in the p-values for all of the variables in the model from those obtained from our selected model.

Appendix 14

Output from the model for the outcome “All co-paid QAACTs sold at <= 1 USD” (allqaactRRP_oneUSD) instead of “All co-paid QAACTs sold at RRP” (allqaactRRP)

allqaactRRP_oneUSD	Linearized					
	Odds Ratio	Std. Err.	t	P> t	[95% Conf. Interval]	
1.identRrp	8.635461	4.019658	4.63	0.000	3.39335	21.97568
1.Owner	1.358621	.3334408	1.25	0.217	.8302629	2.223213
1.healthqualind	1.355021	.3945592	1.04	0.302	.7554177	2.430552
1.urbrur	.8161193	.2996159	-0.55	0.582	.3906746	1.704873
EcolZoneCFS						
2	.9826406	.3405465	-0.05	0.960	.4902006	1.96977
3	1.251216	.6065787	0.46	0.646	.4729859	3.30991
Cat3_PPfpr						
1	1.624427	.5494878	1.43	0.157	.8239669	3.20251
2	1.701506	.6225446	1.45	0.152	.8165437	3.545584
Cat4_NoOfWorkers_auto						
1	.4892435	.1756885	-1.99	0.052	.2379996	1.005713
2	.5205003	.2618968	-1.30	0.200	.1896383	1.428617
3	.3868127	.2518223	-1.46	0.151	.10475	1.428393
typeQWLavail						
2	3.323853	1.57515	2.53	0.014	1.284269	8.602561
3	1.30437	.728368	0.48	0.636	.425367	3.999797
1.AP_QWLprivate	.0475996	.0263899	-5.49	0.000	.0156475	.1447977
Cat3_numberofqaactwithlogo						
1	.3391898	.1057658	-3.47	0.001	.1814264	.6341402
2	.009005	.0082636	-5.13	0.000	.0014281	.0567823
_cons	.1959749	.1626646	-1.96	0.055	.0370554	1.036453

	df	F	P>F
EcolZoneCFS	2	0.13	0.8772
Design	52		

	df	F	P>F
Cat3_PPfpr	2	1.48	0.2376
Design	52		

	df	F	P>F
Cat4_NoOfWorkers_auto	3	1.34	0.2719
Design	52		

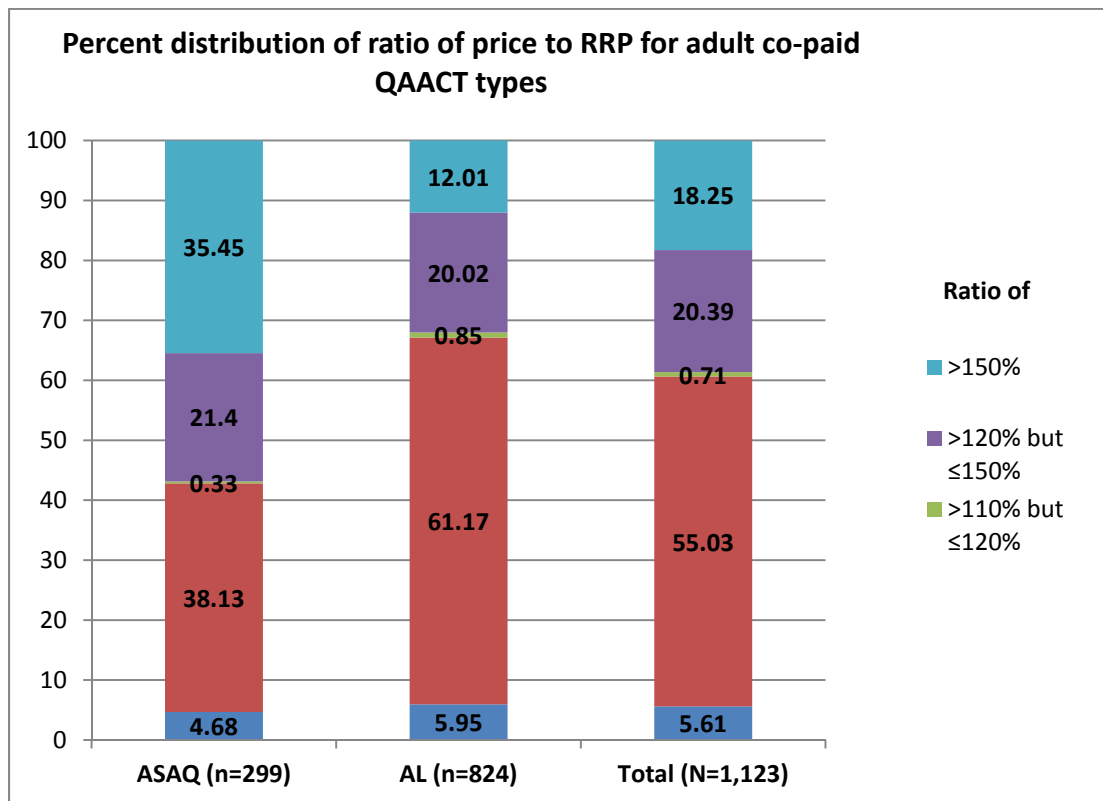
	df	F	P>F
typeQWLavail	2	5.89	0.0050
Design	52		

	df	F	P>F
Cat3_numberofgaactwithlogo	2	15.78	0.0000
Design	52		

Here too there is no change in the p-values for all of the variables in the model from those obtained from our selected model.

Appendix 15

Distribution of actual price per treatment of adult does of co-paid QAACTs

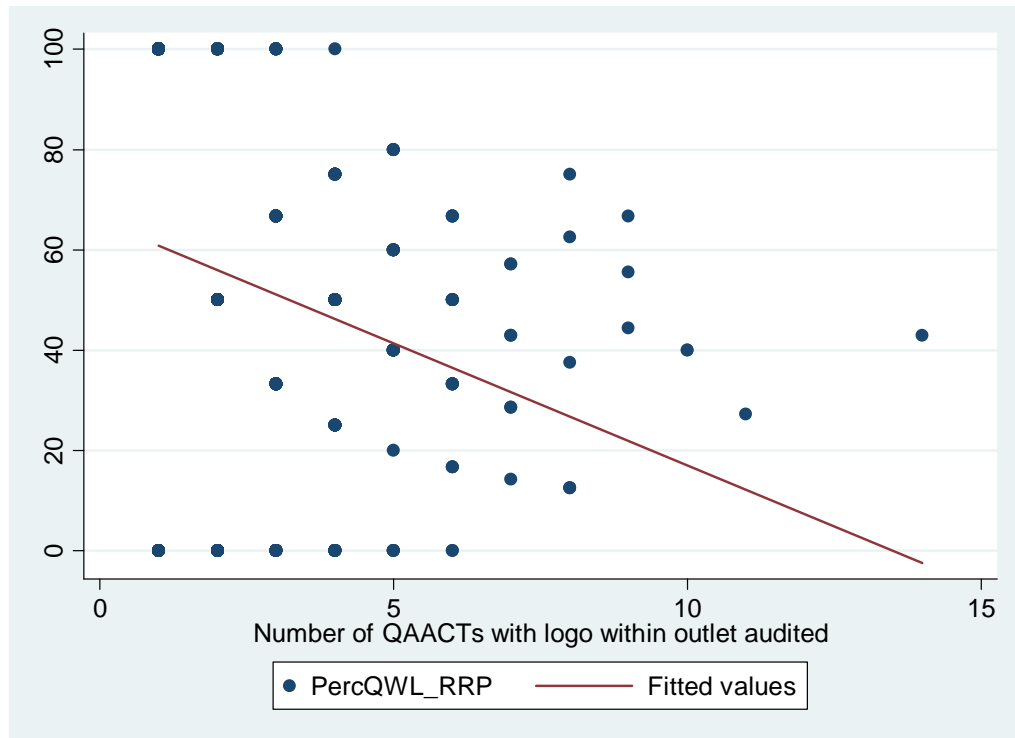


N= Total number of adult co-paid QAACTs audited in private sector

While almost twice as much of AL compared to ASAQ was sold between 90 and 110% of the RRP, more the twice as much ASAQ compared to AL was stocked at >150% of the RRP, signaling a problem with ASAQ.

Appendix 16

Graph showing the relationship between percentage of co-paid QAACTs at RRP and number of co-paid QAACTs per outlet



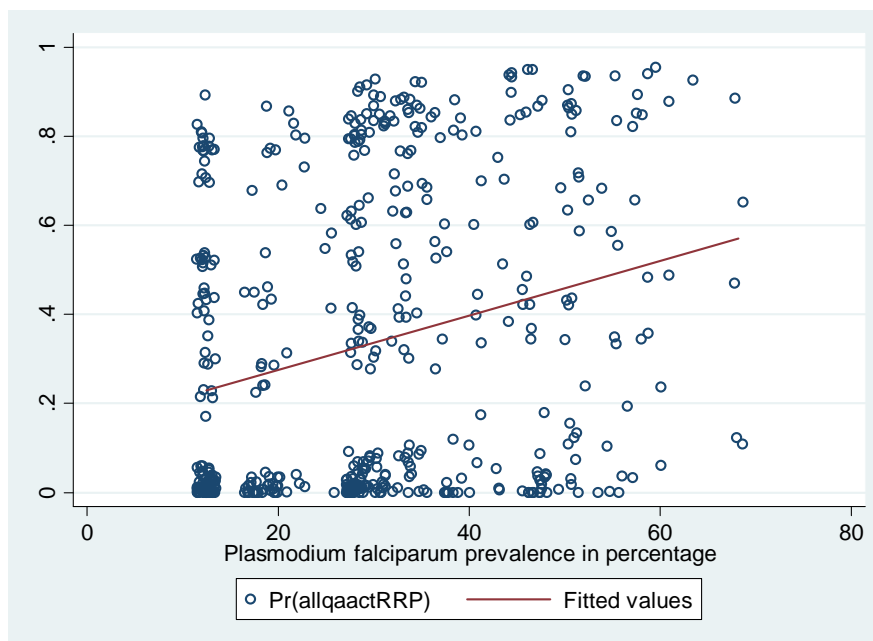
Appendix 17

Jitter plots showing the relationship between the predicted probability of (a) stocking at least 1 co-paid QAACT at RRP, (b) stocking all co-paid QAACT at RRP and malaria prevalence

(a)

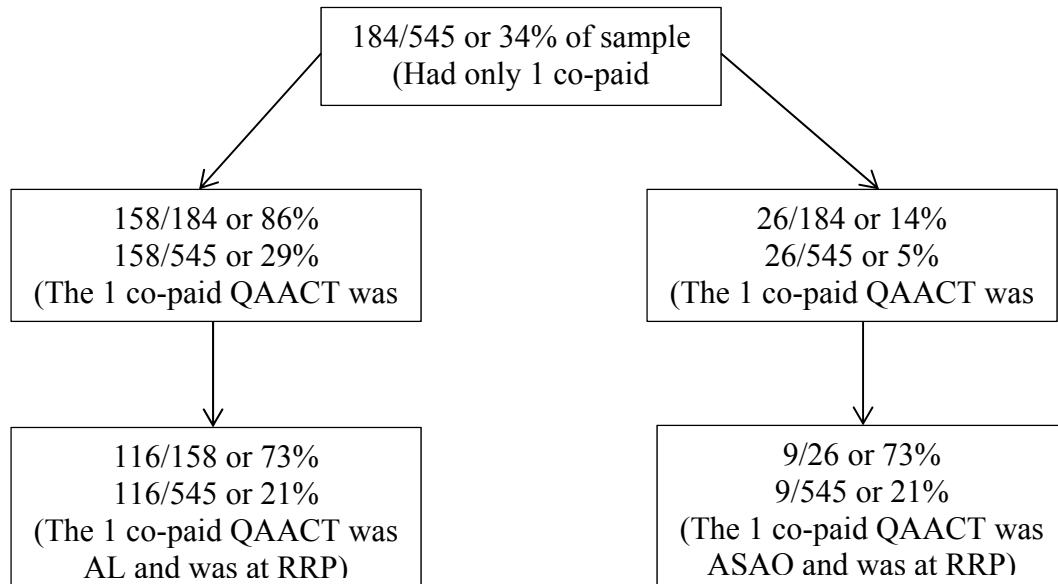


(b)



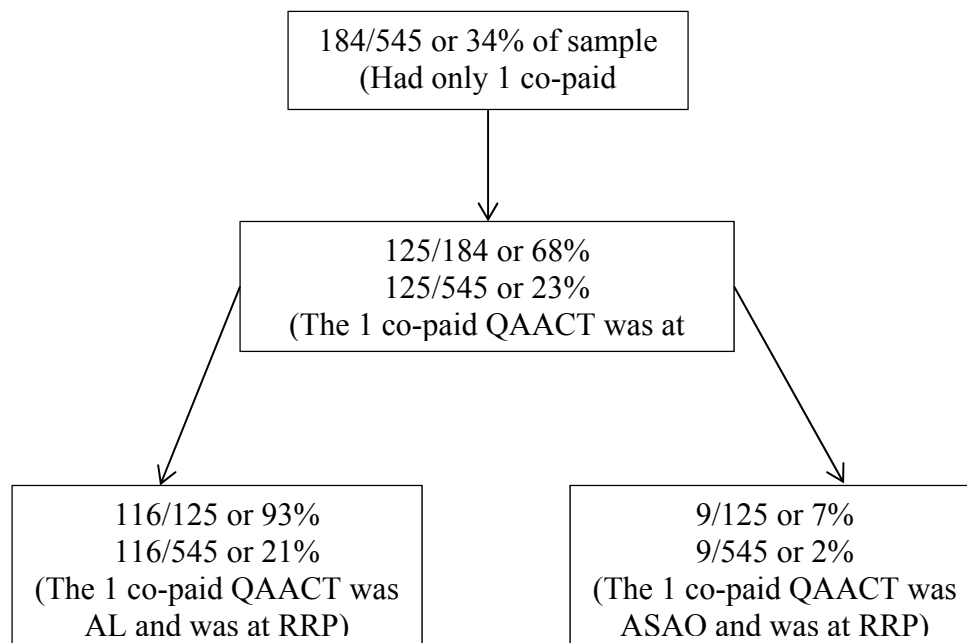
Appendix 18

Distribution of outlets that had only 1 co-paid QAACT at RRP (a)



Appendix 19

Distribution of outlets that had only 1 co-paid QAACT at RRP (b)



Appendix 20

Mean, median (p50), and interquartile range prices per AETD of co-paid ASAQ and AL in our sample

typeQWL		mean	p50	iqr	N
ASAQ		1.725192	1.251238	.9384283	299
AL		1.162543	.9384283	.3128093	830
Total		1.311553	.9384283	.3128093	1129

Appendix 21

Predicted probabilities of knowing the RRP for various outlet characteristics

Predictive margins
Model VCE : Linearized

Number of obs = 542

Expression : Pr(identRrp), predict()

		Delta-method		z	P> z	[95% Conf. Interval]	
		Margin	Std. Err.				
pharmlcs							
	0	.7675388	.0234849	32.68	0.000	.7215091	.8135684
	1	.8355199	.0407303	20.51	0.000	.7556899	.9153498
Cat3_PPfpr							
	0	.8505939	.048611	17.50	0.000	.7553181	.9458697
	1	.7547581	.0442549	17.05	0.000	.66802	.8414962
	2	.7567741	.0403037	18.78	0.000	.6777803	.8357678
EcolZoneCFS							
	1	.7577382	.0528153	14.35	0.000	.6542222	.8612542
	2	.7854747	.0323679	24.27	0.000	.7220347	.8489147
	3	.7681075	.0458777	16.74	0.000	.6781888	.8580261
Cat4_NoOfWorkers_auto							
	0	.8035816	.0329135	24.41	0.000	.7390724	.8680908
	1	.755864	.0241442	31.31	0.000	.7085422	.8031858
	2	.7680387	.0429212	17.89	0.000	.6839146	.8521627
	3	.8378993	.0413728	20.25	0.000	.7568101	.9189885
second							
	0	.6847942	.078031	8.78	0.000	.5318562	.8377322
	1	.7863744	.0243142	32.34	0.000	.7387195	.8340292
healthqualind							
	0	.7769768	.0234426	33.14	0.000	.73103	.8229235
	1	.7643934	.033284	22.97	0.000	.6991579	.8296288
test							
	0	.7738688	.0217525	35.58	0.000	.7312346	.816503
	1	.7802518	.0770506	10.13	0.000	.6292353	.9312683
urbrur							
	0	.6444028	.0471453	13.67	0.000	.5519997	.7368059
	1	.8680627	.0222102	39.08	0.000	.8245314	.9115939
trainedProg							
	0	.6704743	.0335916	19.96	0.000	.604636	.7363126
	1	.8735287	.0213009	41.01	0.000	.8317797	.9152776
urbrur#trainedProg							
	0 0	.3906688	.0797265	4.90	0.000	.2344076	.54693
	0 1	.8511157	.0389453	21.85	0.000	.7747844	.927447
	1 0	.8421236	.0337287	24.97	0.000	.7760166	.9082306
	1 1	.8897528	.0248498	35.81	0.000	.8410481	.9384576

Appendix 22

Adjusted Odds Ratios of Knowing the RRP for Selected Outlet Characteristics

Outlet Characteristics		Knowledge of the RRP	
		Odds Ratio	p-value
Location and Training categories (using urban and untrained as the reference group) [§]	Urban and Untrained	Ref.	-
	Urban and Trained	1.53	0.204
	Rural and Trained	1.07	0.854
	Rural and Untrained	0.10	* <0.001
Type of outlet	Licensed chemical shop	Ref.	0.162
	Pharmacy	1.81	
Falciparum malaria prevalence (%)	Low (10-24)	Ref.	
	Medium (25-34)	0.44	0.342
	High (35-70)	0.44	

*Statistically significant p-value (≤ 0.05)

§This is the interaction (location*training)

Although several variables were included in our model, none of them were significantly associated with our knowing the RRP (including type of private outlet and malaria prevalence), except for training and urban/rural location which were interacted.

For outlets in rural locations, the odds of having knowledge of the RRP was 9 times lower for those without any training compared to urban outlets also with no training ($p<0.001$). The similarity of the two odds ratios (1.53 and 1.07) indicates that training raises outlets in rural locations to an odds ratio of having knowledge of the RRP equivalent to that of outlets in urban locations that had not undergone any training (rural untrained outlets as reference group). Thus, the impact of training on knowledge was only felt in rural areas. We believe that this difference is due to there being many other sources of knowledge of the AMFm beyond training, which are biased towards urban areas so that they already have high knowledge. This allows less room for improvement in knowledge with training in urban areas compared to rural areas.

Appendix 23

Output showing the marginal impact of training for rural outlets as increasing the probability of knowledge by 46% ($p<0.001$), while for urban outlets it was only 4.8% ($p=0.208$)

```
. margins, dydx(trainedProg) at(urbrur=(0 1))

Average marginal effects                                Number of obs   =       542
Model VCE      : Linearized

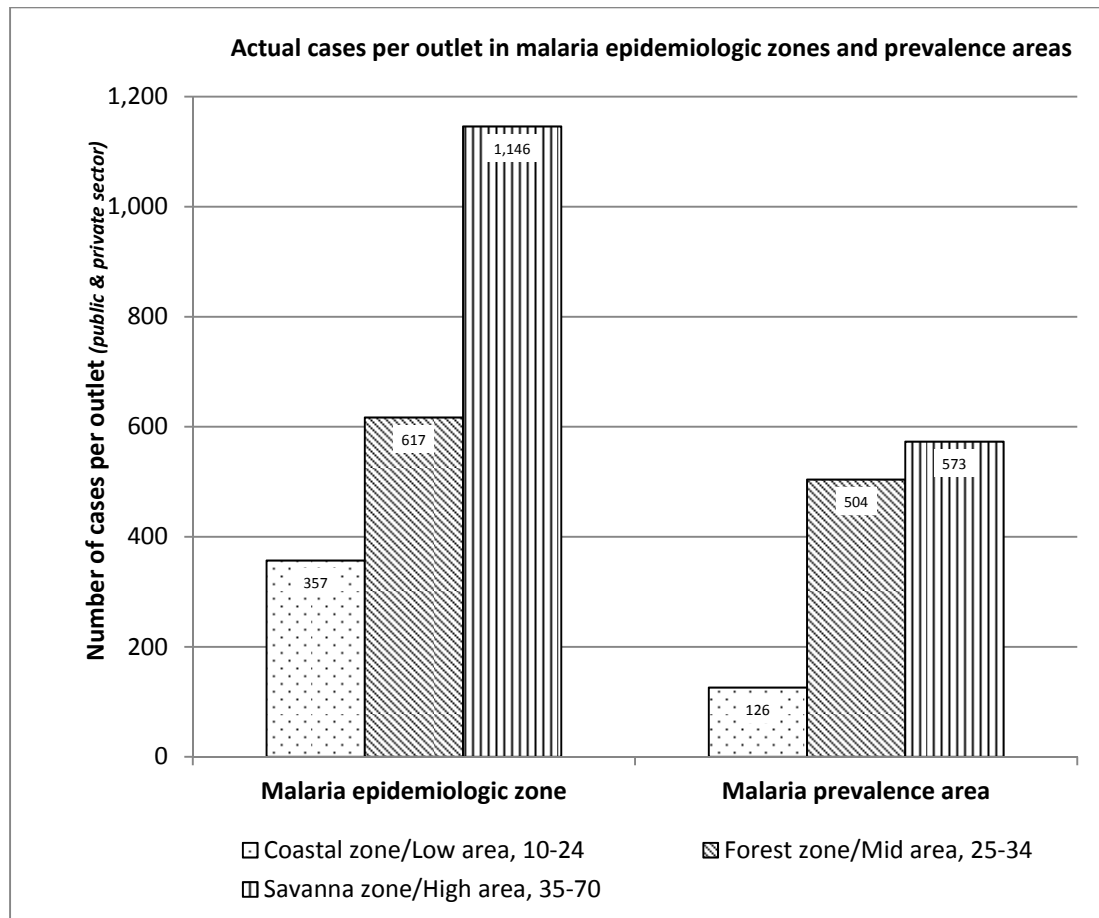
Expression   : Pr(identRrp), predict()
dy/dx w.r.t. : 1.trainedProg

1._at      : urbrur      =          0
2._at      : urbrur      =          1
```

		Delta-method				[95% Conf. Interval]	
		dy/dx	Std. Err.	z	P> z		
1.trainedProg							
	_at						
	1	.4604469	.0761221	6.05	0.000	.3112504	.6096434
	2	.0476292	.0378127	1.26	0.208	-.0264824	.1217409

Note: dy/dx for factor levels is the discrete change from the base level.

Appendix 24



We argue that focusing more knowledge-generating activities in rural and high malaria prevalence areas might not necessarily lead to improved AMFm outcomes. This is so because the high number of cases-per-outlet seen in the high prevalence area and northern savanna zones also suggests that there are simply not enough outlets to serve the cases. Therefore even if all the outlets in the rural and high malaria prevalence areas receive training, malaria will still abound.

Appendix 25

Percentage of the population living in censused “clusters” with outlets with quality assured ACTs in stock at the time of survey, Ghana, 2011.

AMFm IE indicator: Population living in a censused “cluster” where there was at least one of a given type of outlet with a quality-assured ACT in stock at the time of the survey visit (n) as a percentage of the total population living in all the censused “clusters” (N), by location.

	Urban		Rural		Total	
	<i>Percentage (95% CI)</i>	<i>N</i>	<i>Percentage (95% CI)</i>	<i>N</i>	<i>Percentage (95% CI)</i>	<i>N</i>
At least one public health facility stocking quality assured ACTs	28.6 (16.1, 45.5)	363,574	76.7 (60.1, 87.8)	437,796	53.5 (43.1, 63.6)	801,370
At least one private not for profit health facility stocking quality assured ACTs	21.4 (9.3, 42.0)	363,574	23.3 (12.2, 39.9)	437,796	22.4 (13.7, 34.5)	801,370
At least one private for profit outlet stocking quality assured ACTs	100	363,574	90 (74.9, 96.4)	437,796	94.8 (86.7, 98.1)	801,370
At least one community health worker stocking quality assured ACTs	100	363,574	100	437,796	100	801,370
At least one outlet of any type stocking quality assured ACTs	100	363,574	100	437,796	100	801,370

Source: AMFm Phase 1 Independent Evaluation Outlet Survey (Endline)